Pulmonary Embolism after Total Hip Replacement

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PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

1,324 patients were retrospectively studied concerning fatal pulmonary embolism (FPE), which was the most common cause of death within 3 months postoperatively. The incidence of FPE was 0.7 % using thromboembolic prevention with dextran 70. A significant risk factor of FPE was previous orthopaedic surgery. 449 patients were prospectively studied with postoperative scintigraphic screening for PE with a new, dry ^{99m}Tc microaerosol rendering images comparable with the perfusion images in all six projections. The aerosol improved the ventilatory scintigraphic technique but its contribution to the diagnostic accuracy was limited. The diagnosis of pulmonary embolism was not supported by arterial blood gas analyses. Findings in chest radiograms were only of indirect value in diagnosing PE. A standardized, anticoagulative treatment of pulmonary embolism with intermittent heparin and warfarin from the 10th postoperative day, at the earliest, provided hemorrhagic side-effects in 9 %, mostly after heparin administration and in all cases without serious consequencies. No FPE occurred during treatment.

50 patients with scintigraphic abnormalities had a pulmonary angiography within 24 hours. The evaluation disclosed a high PE probability in triangular perfusion defects one segment or larger in size, provided the ventilation in the area was normal or almost normal. Small, sub-segmental perfusion defects, less than half a segment in size, and areas with decreased but not complete loss of perfusion had a low PE probability ($\sim$10 %). 27 lungs had a normal perfusion scintigraphy without PE at angiography. Remaining scintigraphic abnormalities were inconclusive, e.g. perfusion defects with a significantly reduced ventilation, requiring a pulmonary angiography to determine the PE diagnosis.

Acute chest pain in the postoperative course was a significant sign of PE, fatal as well as scintigraphically and angiographically diagnosed.

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PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

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som med vederbörligt tillstånd av Medicinska Fakulteten vid Lunds Universitet för avläggande av medicine doktorsexamen kommer att offentligen försvaras i Universitetsklinikernas Aula, Malmö Allmänna Sjukhus, fredagen den 18 maj 1984 kl. 13.00

av

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leg läk, Mlm

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PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

Hans Fredin

MALMÖ 1984

To

Kristina, Anders, Martin and Thomas

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The present summary is based on the following papers which will be referred to by their Roman numerals:

I. Fredin HO, Nillius SA:
Fatal pulmonary embolism after total hip replacement.
Acta Orthop Scand 1982; 53: 407-11.

II. Fredin HO, Arborelius M Jr:
Scintigraphic evaluation of pulmonary embolism after total hip replacement, using a dry ^{99m}Tc-microaerosol for regional ventilation.
Eur J Nucl Med 1982; 7: 494-9.

III. Fredin HO:
Screening and treatment of pulmonary embolism after total hip replacement.
Acta Orthop Scand 1983; 54: 164-7.

IV. Fredin HO, Arborelius M Jr, Hellekant C:
Scintigraphy and chest radiography in the screening of pulmonary embolism after total hip replacement.
Respiration (in press).

V. Fredin HO, Arborelius M Jr, Hellekant C, Nyman U:
Angiographic evaluation of scintigraphic abnormalities in screening for pulmonary embolism after total hip replacement.
In manuscript form.

Abbreviations and definitions

DVT	=	deep vein thrombosis
FPE	=	fatal pulmonary embolism
HDHE	=	low dose heparin combined with dihydroergotamine
PE	=	pulmonary embolism
PE +	=	positive scintigraphic diagnosis of PE
PE -	=	negative scintigraphic diagnosis of PE
THR	=	total hip replacement.

Scintigraphic defect : No uptake of radioactivity;

Scintigraphic decrease : Obviously reduced but no complete loss of uptake of radioactivity;

FPE : PE diagnosed at autopsy and considered by the pathologist to be the main cause of death;

Angiographic PE : A filling defect or a clear-cut obstruction of a pulmonary artery;

Acute chest pain : A retrospectively recognized attack of acute chest pain as registered in the daily reports.

Background

Pulmonary embolism (PE) is a frequent finding at autopsy. Coon and Coller (1959) registered 13.8 % in 4,391 autopsies during 1954-1959, whereas Morrell and Dunnill (1968) demonstrated PE to be the immediate cause of death in 43 % of all patients with PE and recent emboli to be more frequent in postoperative patients.

In an autopsy study at Malmö General Hospital, Kaij (1959) reported fatal pulmonary embolism (FPE) in 11.5 % of patients deceased at the Department of Orthopaedic Surgery.

Havig (1977) diagnosed macroscopic PE in 55 % and microscopic PE in another 14 % of 508 randomly selected patients. PE was the direct cause of death in 33 % of all cases with PE and a contributing cause in another 19 %. The most proximal origin of fatal emboli was found to be femoral DVT in three out of four patients with DVT in the lower extremities. Also, 55 % of patients with FPE had signs of previous emboli at autopsy.

The frequency of FPE was 0.15 - 1.2 % in a number of reports on various surgical procedures (Schlosser 1977). The frequency was considerably higher, 7-10 %, in patients with hip surgery, especially following fractures, (Sevitt & Gallagher 1959; Zeckert et al. 1974).

Approximately 6,200 total hip replacements (THR) were performed in Sweden (8 million inhabitants) during 1982 (Ahnfelt, L.: Personal communication). Postoperative, thromboembolic complications are common despite prophylaxis. THR patients have previously been studied at Malmö General Hospital. DVT engaging the femoral veins was three times more common in the operated leg and the overall frequency 58 % in the lower extremities as diagnosed by bilateral, ascending phlebography (Nillius & Nylander 1979). PE was registered in about 20 % using pulmonary scintigraphy (Nillius 1978; Bergqvist et al. 1979). FPE has been reported in 2.3 % of 1,174 patients after total hip replacement without thromboprophylaxis (Johnson & Charnley 1977).

The majority of emboli after major surgery are asymptomatic (Williams et al. 1982). According to Dalen and Alpert (1975), the majority of symptomatic pulmonary embolism are unrecognized and untreated. Two to ten per cent of existing PE are diagnosed clinically (Dorr et al. 1979). PE, considered a recurrent disease (Novelline et al. 1978), usually precedes fatal embolism (Freiman et al. 1965; Havig 1977).

The characteristics of thromboembolism after THR are distinguished by the following factors:

(1) THR is usually an elective procedure;

(2) THR implies a fairly uniform type of surgical trauma;

(3) There is a documented high rate of deep vein thrombosis after THR;

(4) The diagnosis of deep vein thrombosis is difficult to determine because of interference from the surgical wound;

(5) The THR patient is partially immobilized postoperatively and during the rehabilitation period;

(6) The THR patient is treated in hospital for periods sufficient for diagnostic procedures.

Aims of the investigation

(1) To study the frequency and the risk factors of FPE in a retrospective series of THR with dextran prophylaxis (I);

(2) To evaluate the significance of acute chest pain as a postoperative symptom of PE (I, II, V);

(3) To study arterial blood gases as a contributional diagnostic sign of postoperative PE (II);

(4) To test the clinical application of a new, dry ^{99m}Tc-microaerosol in ventilation scintigraphies used as a supplement to perfusion scintigraphies in diagnosing PE (II, III, IV, V);

(5) To investigate the effects of a standardized, anticoagulative treatment of PE diagnosed by screening scintigraphies (III);

(6) To evaluate the role of chest radiography in the screening of PE (IV);

(7) To study the significance of different types of scintigraphic perfusion abnormalities by comparison with pulmonary angiography (V);

(8) To evaluate the role of pulmonary scintigraphy in postoperative screening of PE (II, IV, V).

PATIENTS

Over 2,000 THR patients were involved in the present series of studies of whom 449 were included in the prospective groups. The patient material is presented in Table I.

TABLE I

Patients involved in the various studies

Paper	Period	Number	Sex F	Sex M	Age (m ± SD)
I	1969-1978	1,324	831	493	64 ± 10
II	Sept 1979-Nov 1980	189	128	61	64 ± 13
III	Sept 1979-Dec 1981	348	234	114	64 ± 10
IV	Nov 1980-May 1982	210	132	78	67 ± 11
V	Jan 1983-Dec 1983	50	33	17	69 ± 10

All patients were given thromboembolic prevention.

Between 1969 and 1978, when the data were collected for the study on fatal pulmonary embolism (FPE) (I), dextran 70 prophylaxis was the standard procedure.

The effect of thromboembolic prevention was later investigated in separate, randomized studies using dextran 70 and hapten-dextran prophylaxis in comparison with heparin and dihydroergotamine (HDHE) (p. III:1). The patients were randomly allocated to hypotensive and normotensive anaesthesia as well (Fredin et al. in press). Patients with contraindications to hypotensive anaesthesia were randomized to epidural anaesthesia with either dextran 70 or HDHE (Fredin et al. 1984).

PE was less frequent after HDHE prophylaxis in combination with normotensive general anaesthesia, whereas no difference between HDHE and dextran 70 was found in other groups (Table II).

TABLE II

Risk of deep vein thrombosis of the operated leg (DVT) and pulmonary embolism (PE*) in relation to thromboembolic prevention and type of anaesthesia.** (Patients not suitable for randomization to hypotension anaesthesia were given epidural anaesthesia).

	Low dose heparin + dihydroergotamine		Dextran 70
General anaesthesia + hypotension	DVT = 0.46 PE = 0.23		DVT = 0.5 PE = 0.21
General anaesthesia + normotension	DVT = 0.38 PE = 0.04	$p < 0.05$	DVT = 0.58 PE = 0.30
Epidural anaesthesia	DVT = 0.59 (femoral = 0.43) PE = 0.26	$p < 0.05$	DVT = 0.54 (femoral = 0.22) PE = 0.20

* PE diagnosis based on scintigraphy;

** Data from Fredin et al. (1984) and Fredin et al. (in press).

There was a decreased rate of femoral DVT in patients operated upon in epidural anaesthesia and dextran as compared with HDHE.

In the last study (V) the prophylaxis was again dextran 70.

Comment: Previous studies on hemodilution with dextran 70 in THR demonstrated a favourable effect on postoperative PE (Ahlberg et al. 1979; Nillius et al. 1979). As a result, the dose of dextran 70 administered during the day of operation was increased from 500 ml (p. I:2) to 1,000 ml (II, III, IV, V; Fredin et al. 1983; Fredin et al. 1984; Fredin et al. in press; Fredin & Rosberg in manuscript form).

The efficacy of HDHE in prevention of PE could not be demonstrated with any consequence.

Modig et al. (1983) published their observations on thromboembolic complications after THR in high (D 4) - epidural anaesthesia without thromboembolic prevention, demonstrating significantly lower rates of pulmonary embolism when compared with general anaesthesia. The results are in agreement with those of Thorburn et al. (1980).

In a randomized study comparing epidural and general anaesthesia, there was no significant difference in the frequency of PE after THR with dextran prevention (Fredin & Rosberg in manuscript form).

Occurrence of pulmonary embolism

The frequency of PE, based on scintigraphic diagnosis, was in the various studies 20 % (II), 18 % (III) and 20 % (IV), respectively.

Comment: The occurrence rate was almost the same as found by Bergqvist et al. (1980) using pre- and postoperative perfusion scintigraphy, and by Hurson et al. (1979).

Advanced age has been considered an important factor influencing the frequency of PE (Lister 1927; Towbin 1954; Coon & Coller 1959; Anderson et al. 1979; Bell & Simon 1982). Congestive heart failure is also important (Sigel et al. 1979; Bell & Simon 1982; Sasahara et al. 1983) as well as previous pulmonary embolism (Sigel et al. 1979; Sasahara et al. 1983), immobilization (Bell & Simon 1982) and postoperative state (Havig 1977). Other risk factors are malignancy, obesity, polycythemia and pregnancy (Sasahara et al. 1983). Risk factors for PE have not been investigated in the present studies.

Occurrence of fatal pulmonary embolism

The incidence of FPE within three months of surgery was nine out of 1,324 (0.7 %) (p. I:2) in a retrospective series and one out of 348 (0.3 %) in a prospective series (p. III:1).

Comment: The frequency of FPE after THR was reported to be 1.8 % (Crawford et al. 1968), 2.3 % (Bergqvist et al. 1979) and 3.4 % (Coventry et al. 1973) in patients without prevention, and 0.9 % (Crawford et al. 1968), 1.04 % (Johnson et al. 1977) and 1.9 % (Gruber et al. 1980) in patients given thromboembolic prevention. Gruber et al. (1980) and Gruber (1982) did not find any significant difference in a multi-centre study comparing dextran and HDHE.

Thus, the incidence of FPE in the present studies, 0.7 % (I) and 0.3 % (III), was comparatively low but FPE was still the most important cause of death within three months of surgery (I).

The incidence of FPE in the postoperative course depends on the type of thromboembolic prevention, the frequency and accuracy of autopsy (I; Morrell & Dunnill 1968; Havig 1977) as well as the observation time.

Risk factors of fatal pulmonary embolism

A retrospective study (I) was carried out based on clinical records and analysed by multiple regression analysis, comparing nine patients with FPE and a randomly selected group of one hundred patients without FPE.

Sex, age, weight, operated side, type of prosthesis, per- and postoperative blood loss, amount of blood transfusion, and number of previous operations in general or gynaecological surgery did not differ significantly between the group with FPE and the group without. However, previous orthopaedic operations were more common in patients with FPE ($P < 0.05$).

Comment: Age has been reported to be an important risk factor for FPE in non-surgical patients (Coon & Coller 1959; Havig 1977). The effect of age is difficult to study in a group of patients with a fairly homogenous age, such as THR patients.

Acute chest pain

The daily reports were retrospectively searched for notes about acute attacks of chest pain in the postoperative course (I, II, V). Chest pain was significantly more common in patients with FPE ($p < 0.001$) (I), in patients with scintigraphically diagnosed PE ($p < 0.01$) (II) and in patients with angiographically diagnosed PE ($p < 0.05$) (V) as compared with the controls. Eight patients out of 16 with chest pain

had a positive scintigraphic diagnosis of PE (II). In another study comparing scintigraphy and angiography (V), six patients out of 19 with angiographic emboli all had an attack of acute chest pain.

Comment: Bell et al. (1977) reported chest pain to be the most common symptom - 88 % - in patients with clinically suspected PE verified by angiography. Clinical symptoms and signs have been considered non-specific in the diagnosis of PE (Bell et al. 1977; Sasahara et al. 1983). However, in the Urokinase Pulmonary Embolism Trial (1973), dyspnoea was registered as the second most common symptom of PE (84 %). Tachypnoea (> 16/min) was recorded in 92 % of the patients. Apprehension and cough were less frequent and so were raised temperature and tachycardia (> 100/min). Patients in the Urokinase Pulmonary Embolism Trial (1973) and other reports were selected because of symptoms and signs of PE rather than by a screening procedure such as in the present studies (I, II, V).

Arterial blood gases

The analyses of $aB\text{-}PCO_2$ and $aB\text{-}PO_2$ were made with conventional electrodes on blood samples taken prior to the scintigraphy by direct puncture of the radial artery (II).

The results of the arterial blood gas analyses did not differ significantly between patients with PE and those without, not even when selecting patients with PE including two segments or more (p. II:3). Only one patient out of eight with a value of $aB\text{-}PO_2$ below normal (8-13 kPa) had scintigraphic signs of PE.

Comment: Analyses of arterial blood gases have been considered of no value in diagnosing PE (Robin 1977; Bell & Simon 1982; Sasahara et al. 1983). However, Goodall and Greenfield (1980) reported a low $aB\text{-}PCO_2$ as indicative of PE. Also Szucs et al. (1971) found blood gases, especially $aB\text{-}PO_2$, valuable in screening patients suspected of having PE. The combination of hypoxemia, hypocapnia and respiratory alkalosis was also reported to be of some screening value (Szucs et al. 1971). According to Sasahara et al. (1983) there is an inverse relationship between the

level of aB-PO_2 and the extent of the embolism. These studies included only patients with clinical suspicion of PE.

Coagulation factors

Antithrombin III is one of the factors inhibiting coagulation. A decrease of antithrombin III was registered in patients operated on with THR as compared with patients treated with general surgical procedures (Gitel et al. 1979). However, other clinical studies have reported antithrombin III to be an unspecific factor in predicting postoperative thromboembolic complications (Sagar et al. 1976; Fredin et al. 1983).

Anticoagulative treatment

Standardized treatment with heparin and warfarin was given for six weeks to every patient with PE and femoral DVT (p. III:2).

The anticoagulative treatment demonstrated hemorrhagic side-effects in five out of 58 patients (8.5 %). Four had complications during heparin treatment. One patient with multi-segmental emboli had several episodes of hemoptysis after three days on heparin and 12 days postoperatively. Three patients had wound hematoma, one of which ruptured. However, all wounds finally healed without complications. One patient had a large subcutaneous hematoma following venous puncture after nine days on warfarin.

The patients on anticoagulative treatment stayed in hospital for, on average, another five days (range 4-19) until a therapeutic level of prothrombin index had been attained. The hemorrhagic complications in the five patients delayed the discharge by, on average, six days (range 2-19 days). Thus, the anticoagulative treatment with its complications added, on average, 0.9 days of hospitalization, all patients included.

Comment: Heparin treatment has been reported to relieve the bronchial spasm caused by the embolus (Thomas 1965) and to enhance the embolic disintegration by preventing accretion of fibrin platelet layers on the surface of the embolus (Moser et al. 1973). The mortality of untreated PE has varied between 18 and 38 % (Novelline et al. 1978). Untreated patients demonstrated scintigraphic improvement less often and had more new perfusion defects than patients treated with anticoagulants (Secker Walker et al. 1970). Prolonged anticoagulative treatment of PE after THR was reported to reduce the rate of recurrent emboli (Johnson & Charnley 1977). Treatment with heparin and warfarin has previously been advocated (Bell & Simon 1982; Sasahara et al. 1983).

The intermittent way of administrating heparin was chosen as being more convenient to the patient. It has also been reported as more effective in preventing recurrence of PE than the continuous method (Wilson et al. 1981). Clotting tests were not performed in the present studies (Pitney 1970; Salzman et al. 1975). The standard dose of heparin was reduced in patients older than 70 years and/or weighing less than 60 kg (III) (Salzman et al. 1975). The treatment was terminated after six weeks instead of 3-4 months as recommended (Sasahara et al. 1983; Editorial, Lancet 1978). However, a follow-up in one of the present studies after one week of treatment demonstrated a scintigraphic re-perfusion of the abnormal area in 35 out of 36 patients (III).

Pulmonary scintigraphy

The pulmonary scintigraphy was scheduled 10-14 days after surgery. The perfusion and ventilation images were obtained in six projections and recorded on black and white polaroid film (II:3) or on roentgen films (IV).

Perfusion scintigraphy

The perfusion scintigraphy was performed after an I.V. injection of 70-100 MBq of ^{99m}Tc-MAA.

Comment: ^{99m}Tc-MAA has been used in most of the previous perfusion scintigraphy studies.

Ventilation scintigraphy

The ventilation scintigraphy was carried out by inhalation of 70-100 MBq of a dry, ^{99m}Tc-microaerosol of colloidal $Sn(OH)_3$ with a particle size of approximately 0.5 μ (II:1; Arborelius 1982).

Comment: Multiple projections have been advocated since 1967 (Sasahara et al. 1967). The isotope most commonly used for ventilation scintigraphy has been ^{133}Xe. However, the wash-out technique provides only one image, usually in the dorsal projection, and the peripheral resolution is low. The dry ^{99m}Tc-microaerosol has a lower radiation and a higher peripheral resolution than ^{133}Xe. It also renders images in multiple projections comparable to the perfusion images (p. II:3). ^{81}Kr has a short half-life, which makes the isotope unavailable in most hospitals. However, the resolution is high and six projections may be obtained (Goris & Daspit 1981). In the past, aerosols have not been commonly used in clinical practice either due to hard radiation (^{113}In) or to fall-out in the airways (soluble pertechnetate).

Clinical applications

The type, site and area of the perfusion abnormalities were systematically coded and compared with the result of the ventilation scintigraphy. The diagnostic criteria of PE were gradually changed during the investigation (II; IV).

First, screening with perfusion scintigraphy was performed in 189 patients. Patients with a perfusion defect of at least one segment and no sign of lung disease were classified as PE + and patients with small, peripheral abnormalities or a normal perfusion scintigraphy as PE -. Perfusion abnormalities not primarily diagnostic of PE were supplemented with a ventilation scintigraphy and diagnosed as PE + if the ventilation was normal, or as PE - if subnormal (II).

The occurrence of PE was 20 % using this method.

In a second screening study of another 210 patients perfusion plus ventilation scintigraphies were carried out consistently. Every perfusion abnormality with a normal or almost normal ventilation scintigraphy was considered to be PE +. The combination with a more decreased ventilation was classified as PE - (IV).

The rate of PE in this study was also 20 %.

In a third study (V), a sample of 50 patients with perfusion abnormalities had a supplementary pulmonary angiography performed within 24 hours. The emboli involved more than one segmental artery in 16 of 19 patients. The patients' largest perfusion defects corresponded to emboli in 13/13 patients if the defects were multiple, sub-segmental and larger than half a segment, or one segment or larger, without significantly decreased ventilation. No emboli were found in patients with only locally decreased perfusion but in four patients of 15 with abnormally ventilated perfusion defects regardless of size and shape.

Comment: The results of the comparison between scintigraphy and angiography are mainly in accordance with previous reports dealing with non-surgical patients clinically suspected of PE (Moses et al. 1974; McNeil 1976; Biello et al. 1979; Cheely et al. 1981).

The interpretation of the diagnostic procedure in two of the studies (II; IV) would have been somewhat different if the results of the last study (V) had been taken into account. In the clinical study of scintigraphy (II) major perfusion defects would have been studied with ventilation scintigraphy. In the scintigraphic-radiographic study (IV) the small peripheral mismatch defects (code e) would not have been diagnosed as PE. These conclusions are based on the assumption that a pathological scintigraphy is always less reliable than an angiography undertaken within 24 hours. Taking into account the variability of PE, this assumption is not always necessarily true.

Normal perfusion scintigraphy in separate lungs and lobes

In the present comparative study (V) there was no single lung in 27 patients with a normal scintigraphic perfusion and an angiographic embolus. However, 18 lobes in 11 patients had a normal perfusion but an embolus demonstrated at angiography. In five of these 11 patients, scintigraphy and angiography were performed on the same day. The angiography demonstrated a normal blood flow in spite of a contrast filling defect indicating PE. In the remaining six patients the angiography was performed on the following day. The blood flow was normal in seven lobes and markedly reduced or absent in seven.

Comment: The sensitivity of perfusion scintigraphy has been considered close to 100 %, i.e. a negative scintigraphy almost completely excludes PE (Poulose et al. 1970; Gilday et al. 1972; Greenspan 1974; Wagner & Strauss 1975).

Poulose et al. (1970) found normal scintigraphies without specific angiographic signs of PE in 12 patients with clinical symptoms of PE. The findings of Gilday et al. (1972) and Wagner and Strauss (1975) were similar. Greenspan (1974) proposed that a false negative scintigraphy was extremely rare but did not support this statement with data.

The patient materials are small and do not exclude the possibility of a partially occluding embolus as suggested by Greenspan (1974). Moses et al. (1974) presented one patient with an angiographic diagnosis of PE among eight with normal scintigraphies.

The lack of sensitivity in separate lobes (V) may depend on an embolization after the scintigraphy or a non-obstructing embolus. The interval between scintigraphy and angiography is, thus, important for evaluating the real sensitivity of the perfusion scintigraphy.

Chest radiography

In 210 patients with THR, chest radiograms in the postero-anterior and lateral positions were obtained preoperatively and on average 24 hours prior to the scintigraphy. Abnormalities were classified with regard to site, type and compatibility with PE (IV).

The radiographic findings were:

Forty-two signs indicative of PE in 37 patients (18 %), 42 signs of previous lung disease in 42 patients (20 %) and normal findings in 131 patients (62 %). Out of 42 signs indicative of PE, 23 were classified as atelectases and nine as ipsilateral elevation of the diaphragm (IV:7). There was a poor correlation between chest radiography and scintigraphy regarding PE.

Chest radiography was made in 50 patients postoperatively and prior to a pulmonary angiography (V). The chest radiograms were normal in the embolic area of all patients.

Comment: Abnormalities in the chest radiogram of patients with angiographic PE are common (Moses et al. 1974) but considered non-specific (Bell & Simon 1982). Such changes also occur in patients with cardiovascular diseases. We found lamellar atelectasis to be the most frequent indirect sign in patients with scintigraphic PE (5/41 - 12 %) compared with a frequency of 11 out of 41 (27 %) in a study by Moses et al. (1974). In the latter study as in others, the patients had presented clinical symptoms rather than being identified by a screening procedure.

Pulmonary infarction in PE is usually incomplete (Hampton & Castleman 1940) and therefore reversible within a few days (Fleischner 1967). However, it may impair the perfusion as well as the ventilation scintigraphy (code -) and the diagnosis may consequently be missed.

Chest radiography was only of indirect value in diagnosing postoperative PE (V).

Pulmonary angiography

Bilateral, selective pulmonary angiography was performed in 50 patients with percutaneous catheterization of the femoral vein (Seldinger 1953) using a pigtail catheter (V). Either iohexol, calcium/sodium metrizoate or ioxaglate was injected at a rate of 25 ml/s. The images were obtained in two to three projections, mostly documented by cine-recordings. No complication occurred. Diagnostic criteria of pulmonary embolism were a constant intraluminal filling defect on multiple films and sharp cut-offs of vessels (Dalen et al. 1971). Other signs were regarded as non-specific.

Comment: Superselective injections and magnification technique can demonstrate pulmonary emboli or vessel cut-offs as small as 0.5 mm in diameter, which decreases the risk of missing significant emboli (Novelline et al. 1978). Cine-recording also decreases the importance of patient cooperation and permits a dynamic documentation, however, not with as high a peripheral resolution as with the cut-film technique.

A morbidity rate of approximately 5 % has been reported after pulmonary angiography and a mortality rate of approximately 0.5 % (Moses et al. 1974; Mills et al. 1980). However, data are not available concerning the frequency of side-effects after pulmonary angiography using modern technique with pigtail catheters (Mills et al. 1980) and low osmolality contrast media (Almén et al. 1975). Also, the use of angioscope, cine-recording and preliminary video-interpretation is faster as compared with the conventional technique of serial cut-films.

GENERAL DISCUSSION

Prognosis of PE

One aspect of the early prognosis after PE concerns the resolution of emboli, which is most likely to occur in recent emboli not yet organized (Freiman et al. 1965; Sautter et al. 1967; Dalen & Alpert 1975). Resolution may be enhanced by heparin treatment. Moser et al. (1973) demonstrated in dogs that experimental emboli in vivo decreased significantly in size after three and six hours in all animals but more rapidly after heparin administration.

Resolution of emboli has been verified by angiography after 7-19 days (Fred et al. 1966) and even as early as 30 hours after the diagnosis (Sautter et al. 1967). Scintigraphic reperfusion in clinically selected patients with PE was demonstrated by Tow and Wagner (1967), Secker Walker et al. (1970) and Winebright et al. (1970) after a few days and up to 2-3 weeks. Winebright et al. (1970) reported that a complete resolution, even with heparin, neither occurred later than the 20th day nor in patients above the age of 60. In the present investigation several of the scintigraphies demonstrated complete reperfusion after one week of heparin treatment in spite of the patients' advanced age (II, III). In the Urokinase Pulmonary Embolism Trial (1973), follow-up scintigraphy demonstrated a resolution of 56 % after 14 days and 75 % after three months, but rarely later.

The most important effect of treatment of PE is probably the prevention of further emboli (Bauer 1946; Barritt & Jordan 1960).

It must be remembered, however, that recurrence of PE may occur during heparin treatment (I, II; Winebright et al. 1970; Paraskos et al. 1973; Salzman et al. 1975). Delayed death after PE is due to recurrent embolism rather than persistence of the original embolus (Oakley 1968).

The late prognosis is dependent on the cardiac status prior to the embolic episode (Paraskos et al. 1973). Chronic pulmonary hypertension is a rare type of complication but may occur in patients with recurrent embolism left untreated (Dalen & Alpert 1975; Editorial, Lancet 1978).

Thromboembolic prevention

Thromboembolic prophylaxis is indicated in every patient undergoing major orthopaedic surgery. In several reports dextran 70 has been documented as an effective drug, especially concerning fatal PE (Bergentz 1978; Ljungström 1983). The side-effects are few. Major hemorrhages are probably fewer than after prophylaxis with low dose heparin plus dihydroergotamine (Fredin et al. 1984). Anaphylactic reactions after dextran can be significantly decreased by the prophylactic use of hapten-dextran (dextran 1 15 %, Pharmacia AB, Uppsala, Sweden) (Renck et al. 1983). The reduction of this type of complication has made it possible to study the significance of preoperative administration of dextran 70, which for theoretical reasons can be assumed to further improve the prophylactic effect of dextran.

Thus, it seems today as if thromboembolic prophylaxis in total hip replacement with dextran 70 is an effective method with few side-effects and easy to carry out within the daily routine.

Diagnostic procedure

The most specific methods for detecting DVT and PE, i.e. ascending phlebography and pulmonary angiography, are invasive and therefore not suitable for screening procedures. The fibrinogen uptake method is useful but not specific for the detection of DVT in the operated area due to interference from the wound hematoma.

Pulmonary scintigraphy, used as a postoperative screening procedure, is mainly useful for excluding PE. In some instances, major scintigraphic defects are diagnostic of PE. However, approximately 10 % of the total number of patients have inconclusive findings which require

an angiography to determine a definite diagnosis. Intravenous pulmonary angiography with digital subtraction may replace conventional angiography in future (Pond et al. 1983), if the diagnostic accuracy turns out to be adequate. This procedure, which is less invasive, may facilitate a diagnostic screening procedure of postoperative PE.

It must be remembered, however, that PE is a recurrent disease. Thus, a negative diagnosis of PE is valid at only that precise moment. Scintigraphy should therefore be repeated if new symptoms or signs occur.

Treatment of PE

Adequate anticoagulative treatment of PE, and DVT, is known to decrease the risk of recurrence. Treatment of PE basically implies a treatment of the thrombotic disease.

Thromboembolic complications are frequent after THR despite thromboembolic prevention. DVT of the lower extremities was diagnosed in approximately 60 % of the patients (Nillius & Nylander 1979) and PE in 15-20 % (II, III, IV).

In most patients the natural fibrinolysis is usually sufficient to counteract thromboembolic complications. However, factors that increase the risk such as advanced age, surgery and immobilization are present in all THR patients. Therefore, the fibrinolytic system has to be supported in some patients despite an optimal thromboembolic prevention. Anticoagulative treatment with warfarin had few complications and demanded laboratory controls only once a week (III).

Thus, it would be possible to combine dextran prophylaxis with a "prolonged prevention" or an "early treatment" of postoperative thromboembolic complications with warfarin administered as therapeutically effective from the 10th postoperative day until 6-12 weeks. Such treatment would provide an optimal safety against thromboembolic complications at a reasonable cost, compared with diagnostic procedures, and would not prolong the stay in hospital.

CONCLUDING REMARKS

(1) Fatal pulmonary embolism was the most common cause of immediate death following total hip replacement.

The frequency of fatal pulmonary embolism may be maintained below 1 % with dextran prophylaxis.

The only significant risk factor of fatal pulmonary embolism was previous orthopaedic operations.

(2) Acute chest pain in the postoperative course was a significant sign of pulmonary embolism, fatal as well as scintigraphically and angiographically diagnosed.

(3) Arterial blood gas analyses did not contribute to the diagnosis of pulmonary embolism.

(4) The new, dry ^{99m}Tc microaerosol provided an improvement in the ventilatory scintigraphic technique. However, its contribution to diagnostic accuracy was limited.

(5) A standardized, anticoagulative treatment of pulmonary embolism with heparin and warfarin from the 10th postoperative day, at the earliest, gave hemorrhagic side-effects in 9 % of the patients, none being serious. These mostly occurred after heparin administration. No fatal pulmonary embolism occurred during treatment.

(6) Most signs of pulmonary embolism in chest radiograms were unspecific. Chest radiography was only of indirect value and not mandatory in the diagnostic process of postoperative PE.

(7) Perfusion defects at least one segment in size with normal or slightly decreased ventilation have a high probability of PE, whereas perfusion decreases or small, peripheral defects less than half a segment in size have a low probability. Single or multiple sub-segmental, triangular perfusion defects, larger than half a segment, with normal or almost normal ventilation may have a high probability of PE. However, further documentation is required. Perfusion defects with significantly decreased ventilation are inconclusive findings.

(8) Pulmonary scintigraphy may be used for postoperative screening of pulmonary embolism. However, pulmonary angiography is a necessary supplement in order to determine the diagnosis in patients with inconclusive scintigraphic findings. Pulmonary scintigraphy will not detect some of the emboli which do not interfere with the blood flow. The result of a pulmonary scintigraphy is valid only at the time of the examination.

Thromboembolic prevention using dextran 70

Twenty millilitres of Promiten^{R} (dextran 1 15 %; Pharmacia AB, Uppsala, Sweden) is administered I.V. for 2-5 minutes, no later than 15 minutes before the first infusion of dextran 70; 500 ml of dextran 70 (Macrodex^{R} 6 % in saline or glucose solution; Pharmacia AB, Uppsala, Sweden) is given during the operation and another 500 ml during the rest of the operation day; 500 ml is also given on the first and third postoperative days, as well as on the second day, if the peroperative blood loss exceeds 2,000 ml. If the patient is not adequately mobilized another 500 ml is given on the fifth day.

Diagnosis of pulmonary embolism by scintigraphy/angiography

PE is likely if the largest abnormality is a triangular perfusion defect of at least one segment in size and the hypoperfused area has a normal or almost normal ventilation.

PE can be excluded if the perfusion scintigraphy is normal.

PE is unlikely if the perfusion scintigraphy demonstrates small, subsegmental (< 50 %) perfusion defects or areas with decreased but not complete loss of perfusion (probability approximately 10 %).

PE can neither be diagnosed nor excluded if the scintigraphic abnormalities are inconclusive, e.g. perfusion defects combined with significantly reduced ventilation. Pulmonary angiography is then mandatory to determine the PE diagnosis.

Anticoagulative treatment with heparin-warfarin

Treatment is started no earlier than on the 10th postoperative day by an I.V. administration of 7,500 IU of sodium heparin six times per day. The dose is reduced in patients over the age of 70 and in patients weighing less than 60 kg.

The heparin treatment is discontinued when the prothrombin complex has reached a therapeutic level following peroral administration of warfarin. Warfarin is given in a dose of 12.5, 10 and 7.5 mg during the first three days to patients with a prothrombin complex above 90 %. The prothrombin complex is measured once a week after a steady state has been attained. The treatment is terminated after 6-12 weeks.

If the treatment must be started before the 10th day, 500 ml of dextran 40 (Rheomacrodex^{R}, 4 % in saline, Pharmacia AB, Uppsala, Sweden) is infused daily until the warfarin treatment has become therapeutically effective by the 10th day.

Pulmonary embolism and deep vein thrombosis engaging the femoral segment are treated with heparin-warfarin for 6-8 weeks, irrespective of symptoms or signs, whereas deep vein thrombosis of the lower leg is given heparin for one week.

REFERENCES

Ahlberg Å, Nillius A, Rosberg B, Wulff C. Preoperative normovolemic hemodilution in total hip replacement - A clinical study. Acta Chir Scand 1979;143:407.

Almén T, Aspelin P, Levin B. Effect of ionic and non-ionic contrast medium on aortic and pulmonary arterial pressure: An angiocadiographic and rabbits. Invest Radiol 1975;10: 519-25.

Anderson L, Kammerer WS, Greer RB III. Risk factor assessment in 101 total hip arthroplasties. Clin Orthop 1979;141:50-4.

Arborelius M Jr. Generation of a microaerosol suitable for deposition in the peripheral airways. Eur J Respir Dis (Suppl) 1982;119:19-27.

Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet 1960;1: 1309-12.

Bauer G. Thrombosis. Early diagnosis and abortive treatment with heparin. Lancet 1946;1:447-54.

Bell WR, Simon TL. Current status of pulmonary thromboembolic disease: Pathophysiology, diagnosis, prevention, and treatment. Am Heart J 1982; 103:239-62.

Bell WR, Simon TL, DeMets DL. The clinical features of submassive and massive pulmonary emboli. Am J Med 1977;62:355-60.

Bergentz SE. Dextran in prophylaxis of pulmonary embolism. World J Surg 1978; 2: [illegible].

Bergqvist D, Efsing HO, Hallböök T, Hedlund T. Thromboembolism after elective and post-traumatic hip surgery - A controlled prophylactic trial with dextran 70 and low-dose heparin. Acta Chir Scand 1979;145:213-18.

Bergqvist D, Efsing HO, Hallböök T, Lindblad B. Prevention of postoperative thromboembolic complications. A prospective comparison between dextran 70,dihydroergotamin heparin and a sulphated polysaccharid. Acta Chir Scand 1980;146: 559-68.

Biello DR, Mattar AG, McKnight RC, Siegel BA. Ventilation-perfusion studies in suspected pulmonary embolism. AJR 1979; 173: 1033-7.

Cheely R, McCartney WH, Perry JR, Delany DJ, Bustad L, Wynia VH, Griggs TR. The role of noninvasive tests versus pulmonary angiography in the diagnosis of pulmonary embolism. Am J Med 1981;70:17-22.

Coon WW, Coller FA. Some epidemiologic considerations of thromboembolism. Surg Gynecol Obstet 1959;109:487-501.

Coventry MB, Nolan DR, Beckenbaugh RD. "Delayed" prophylactic anticoagulation: A study of results and complications in 2,012 total hip arthroplasties. J Bone Joint Surg (Am) 1973; 55-A:1487-92.

Crawford WJ, Hillman F, Charnley J. A clinical trial of prophylactic anticoagulant therapy in elective hip surgery. Internal Publication No. 14, May 1968; Centre for Hip Surgery, Wrightington Hospital, Wiggan, England.

Dalen JE, Alpert JS. Natural history of pulmonary embolism. Prog Cardiovasc Dis 1975;17:259-70.

Dalen JE, Brooks HL, Johnson LW, Meister SG, Szucs MM Jr, Dexter L. Pulmonary angiography in acute pulmonary embolism: Indications, techniques, and results in 367 patients. Am Heart J 1971;81:175-85.

Dorr LD, Sakimura I, Mohler JG. Pulmonary emboli following total hip arthroplasty: Incidence study. J Bone Joint Surg 1979; 61A:1083-6.

Editorial, Lancet 1978;1:194-195.

Fleischner FG. Roentgenology of the pulmonary infarct. Semin Roentgenol 1967;2:61-76.

Fred HL, Axelrad MA, Lewis JM, Alexander JK. Rapid resolution of pulmonary thromboemboli in man. An angiographic study. JAMA 1966;196:121-3.

Fredin H, Gustafson C, Rosberg B. Hypotensive anesthesia, thromboprophylaxis and postoperative thromboembolism in total hip arthroplasty. Acta Anaesth Scand (in press).

Fredin H, Nilsson B, Rosberg B, Tengborn L. Pre- and postoperative levels of antithrombin III with special reference to thromboembolism after total hip replacement. Thromb Haemost 1983;49:158-161.

Fredin H, Rosberg B. Thromboembolism and anesthetic techniques in total hip arthroplasty. A controlled study of general anaesthesia and epidural analgesia. (In manuscript form).

Fredin H, Rosberg B, Arborelius M Jr, Nylander, G. On thromboembolism after total hip replacement in epidural analgesia. A controlled study of dextran 70 and low-dose heparin combined with dihydroergotamine. Br J Surg 1984; 71:58-60.

Freiman DG, Suyemoto J, Wessler S. Frequency of pulmonary thromboembolism in man. N Engl J Med 1965;272:1278-80.

Gilday DL, Poulose KP, DeLand FH. Accuracy of detection of pulmonary embolism by lung scanning correlated with pulmonary angiography. AJR 1972;115:732-8.

Gitel SN, Salvati EA, Wessler S, Robinson HJ Jr, Worth MH Jr. The effect of total hip replacement and general surgery on antithrombin III in relation to venous thrombosis. J Bone Joint Surg (Am) 1979;61-A:653-6.

Goodall RJR, Greenfield LJ. Clinical correlations in the diagnosis of pulmonary embolism. Ann Surg 1980;191:219-23.

Goris ML, Daspit SG. Krypton-81m ventilation scintigraphy for the diagnosis of pulmonary emboli. Clin Nucl Med 1981; 6:207-12.

Greenspan RH. Does a normal isotope perfusion scan exclude pulmonary embolism? Invest Radiol 1974;9:44-6.

Gruber UF. Prevention of fatal postoperative pulmonary embolism by heparin dihydroergotamine or Dextran 70. Br J Surg 1982;69:(Suppl):S54-8.

Gruber UF, Saldeen T, Brokop T, Eklöf B, Eriksson I, Goldie I, Gran L, Hohl M, Jonsson T, Kristersson S, Ljungström KG, Lund T, Maartman Moe H, Svensjö E, Thomson D, Torhorst J, Trippestad A, Ulstein M. Incidences of fatal postoperative pulmonary embolism after prophylaxis with dextran 70 and low-dose heparin: an international multicentre study. Br Med J 1980;280:69-72.

Hampton AO, Castleman B. Correlation of postmortem chest teleroentgenograms with autopsy findings with special reference to pulmonary embolism and infarction. AJR 1940; 43:305-26.

Havig Ö. Deep vein thrombosis and pulmonary embolism. Acta Chir Scand 1977;Suppl 478.

Hurson B, Ennis JT, Corrigan TP, MacAuley P. Dextran prophylaxis in total hip replacement: A scintigraphic evaluation of the incidence of deep vein thrombosis and pulmonary embolus. Ir J Med Sci 1979;148:140-4.

Johnson R, Charnley J. Treatment of pulmonary embolism in total hip replacement. Clin Orthop 1977;124:151-54.

Johnson R, Green JR, Charnley J. Pulmonary embolism and its prophylaxis following the Charnley total hip replacement. Clin Orthop 1977;127:123-32.

Kaij K. Tromboembolifrekvensen i ett obduktionsmaterial. Läkartidningen 1959;53:1437-43.

Lister WA. A statistical investigation into the causation of pulmonary embolism following operation. Lancet 1927;1: 111-6.

Ljungström KG. Dextran prophylaxis of fatal pulmonary embolism. World J Surg 1983;7:767-72.

McIntyre KM, Sasahara AA. Angiography, scanning, and hemodynamics in pulmonary embolism: critical review and correlations. Crit Rev Radiol Sci 1972;3:489-521.

McNeil BJ. A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism. J Nucl Med 1976;17:613-6.

Mills SR, Jackson DC, Older RA, Heaston DK, Moore AV. The incidence, etiologies, and avoidance of complications of pulmonary angiography in a large series. Radiology 1980; 136:295-9.

Modig J, Borg T, Karlström G, Maripuu E, Sahlstedt B. Thromboembolism after total hip replacement: Role of epidural and general anesthesia. Anesth Analg 1983;62:174-80.

Morrell T, Dunnill MS. The post-mortem incidence of pulmonary embolism in a hospital population. Br J Surg 1968;55: 347-52.

Moser KM, Guisan M, Bartimmo EE, Longo AM, Harsanyi PG, Chiorazzi N. In vivo and post mortem dissolution rates of pulmonary emboli and venous thrombi in the dog. Circulation 1973; 48:170-8.

Moses DC, Silver TM, Bookstein JJ. The complementary roles of chest radiography, lung scanning, and selective pulmonary angiography in the diagnosis of pulmonary embolism. Circulation 1974;49:179-88.

Nillius SA. On thromboembolism after total hip replacement. Thesis, University of Lund, 1978.

Nillius SA, Ahlberg A, Arborelius M Jr, Rosberg B. Preoperative normovolaemic haemodilution with dextran 70 as a thromboembolic prophylaxis in total hip replacement. Int Orthop 1979;3:197-202.

Nillius SA, Nylander G. Deep vein thrombosis after total hip replacement: a clinical and phlebographic study. Br J Surg 1979; 66:324-6.

Novelline RA, Baltarowich OH, Athanasoulis CA, Waltman AC, Greenfield AJ, McKusick KA. The clinical course of patients with suspected pulmonary embolism and a negative pulmonary arteriogram. Radiology 1978; 126: 561-7.

Oakley CM. Conservative management of pulmonary embolism. Br J Surg 1968;55:801-5.

Paraskos JA, Adelstein SJ, Smith RE, Rickman FD, Grossman W, Dexter L, Dalen JE. Late prognosis of acute pulmonary embolism. N Engl J Med 1973;289:55-8.

Pitney WR. Annotation: Heparin therapy and its laboratory control. Br J Haematol 1970;18:499-502.

Pond GD, Ovitt TW, Capp MP. Comparison of conventional pulmonary angiography with intravenous digital subtraction angiography for pulmonary embolic disease. Radiology 1983; 147:345-50.

Poulose KP, Reba RC, Gilday DL, DeLand FH, Wagner HN Jr. Diagnosis of pulmonary embolism. A correlative study of the clinical, scan, and angiographic findings. Br Med J 1970; 3:67-71.

Renck H, Ljungström KG, Hedin H, Richter W. Prevention of dextran-induced anaphylactic reactions by hapten inhibition. Acta Chir Scand 1983;149:355-60.

Robin ED. Overdiagnosis and overtreatment of pulmonary embolism: The emperor may have no clothes. Ann Int Med 1977;87: 775-81.

Sagar S, Stamatakis JD, Higgins AF, Nairn D, Maffei FH, Thomas DP, Kakkar VV. Efficacy of low-dose heparin in prevention of extensive deep-vein thrombosis in patients undergoing total-hip replacement. Lancet 1976;1:1151-4.

Salzman EW, Deykin D, Shapiro RM, Rosenberg R. Management of heparin therapy. Controlled prospective trial. N Engl J Med 1975;292:1046-50.

Sasahara AA, Belko JS, Simpson RG. Multiple-view lung scanning. J Nucl Med 1967;9:187-91.

Sasahara AA, Sharma GVRK, Barsamian EM, Schoolman M, Cella G. Pulmonary thromboembolism. Diagnosis and treatment. JAMA 1983;249:2945-50.

Sautter RD, Fletcher FW, Ousley JL, Wenzel FJ. Extremely rapid resolution of a pulmonary embolus. Report of a case. Dis Chest 1967;52:825-7.

Schlosser V. Klinik, Prophylaxe und Therapie der Lungenembolie aus chirurgischer Sicht. Med Klin 1977;72:1947-58.

Secker Walker RH, Jackson JA, Goodwin J. Resolution of pulmonary embolism. Br Med J 1970;4:135-9.

Seldinger SI. Catheter replacement of the needle in percutaneous arteriography. Acta Radiol 1953; 39:368-76.

Sevitt S, Gallagher NG. Prevention of venous thrombosis and pulmonary embolism in injured patients. Lancet 1959;2: 981-9.

Sigel B, Justin JR, Gibson RJ, Felix WR Jr, Popky GL, Parker JA, Ipsen J. Risk assessment of pulmonary embolism by multivariate analysis. Arch Surg 1979;114:188-92.

Szucs MM Jr, Brooks HL, Grossman W, Banas JS Jr, Meister SG, Dexter L, Dalen JE. Diagnostic sensitivity of laboratory findings in acute pulmonary embolism. Ann Int Med 1971; 74:161-6.

Thomas DP. Treatment of pulmonary embolic disease. A critical review of some aspects of current therapy. N Engl J Med 1965;273:885-892.

Thorburn J, Louden JR, Vallance R. Spinal and general anaesthesia in total hip replacement: Frequency of deep vein thrombosis. Br J Anaesth 1980;52:1117-21.

Tow DE, Wagner HN Jr. Recovery of pulmonary arterial blood flow in patients with pulmonary embolism. N Engl J Med 1967; 276:1053-9.

Towbin A. Pulmonary embolism. Incidence and significance. JAMA 1954;156:209-15.

UPET (The Urokinase Pulmonary Embolism Trial). A National Cooperative Study. Circulation 1973;47:Suppl 2:7.

Wagner HN Jr, Strauss HW. Radioactive tracers in the differential diagnosis of pulmonary embolism. Prog Cardiovasc Dis 1975; 17:271-82.

Williams JW, Eikman EA, Greenberg S. Asymptomatic pulmonary embolism. A common event in high risk patients. Ann Surg 1982; 195:323-7.

Wilson JE III, Bynum LJ, Parkey RW. Heparin therapy in venous thromboembolism. Am J Med 1981;70:808-16.

Winebright JW, Gerdes AJ, Nelp WB. Restoration of blood flow after pulmonary embolism. Arch Intern Med 1970;125:241-7.

Zeckert F, Kohn P, Vormittag E, Poigenfürst J, Thien M. Thromboemboliprophylaxe mit Acetylsalicylsäure bei Operationen wegen hüftgelenksnaher Frakturen. Monatsschr Unfallheilk 1974;77: 97-110.

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FATAL PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

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A retrospective study of fatal pulmonary embolism (FPE) was carried out in 1,324 cases of total hip replacement (THR), performed during 1969 to 1978. Dextran 70 (Macrodex® 6 per cent in saline, Pharmacia AB, Sweden) was given as thromboembolic prophylaxis. Sixteen patients died within 3 months. Autopsy was performed in 14 cases. Nine died from embolism, which makes an incidence of 0.7 per cent. Autopsy was performed in 8 of these cases. Seven patients died during the second and third week. Five patients had complained of acute chest pain and 4 of them had chest radiograms taken, which were normal. Only one patient had clinical symptoms of deep vein thromboses. Perfusion lung scan was performed as a screening procedure in 3 cases, all of them showing defects typical of pulmonary embolism. Four patients died from FPE, despite heparin therapy for 3–5 days. A comparison between patients with FPE and a control group showed that premonitory attacks of acute chest pain and previous operations for orthopaedic reasons were significantly more common in patients with FPE ($P < 0.001$ and $P < 0.05$), respectively). No difference could be found between the groups concerning blood loss, amount of transfusion, sex, operated side, type of prosthesis and weight.

Key words: hip joint (surgery); pulmonary embolism

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There is mounting evidence that the frequency of venous thromboembolic complications in the postoperative period is increasing in the Western world (Hume et al. 1970). The most plausible reason is the improvement of anaesthetic and operative techniques which have made it possible to perform successful major surgery in elderly people. This applies especially to total hip replacement (Cavendish & Charnley 1972).

Approximately 80 per cent of pulmonary emboli arise without premonitory symptoms of peripheral venous thromboses (Kakkar 1977). Studies of autopsies have shown that most cases of pulmonary embolism are not diagnosed during life and therefore not treated (Fitts et al. 1964, Freiman et al. 1965). Death from attacks of major pulmonary embolism occurs in two-thirds of the cases within 30 minutes of the embolic event, a period too short for successful therapy (Donaldson et al. 1963). Thromboprophylaxis has thus become a necessity in the prevention of fatal embolism in high-risk patients. The incidence of FPE after THR without thromboprophylaxis varies between 1.8 and 3.4 per cent (Salzman & Harris 1976).

The purpose of this study was to determine the incidence of FPE within 3 months after THR with dextran prophylaxis. Furthermore, we wanted to determine possible operative risk factors for pulmonary embolism as well as the significance of acute chest pain as a premonitory symptom.

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PATIENTS AND METHODS

During 1969 to 1978 a total of 1,324 hips were operated on and THR performed by several senior surgeons at the Department of Orthopaedic Surgery, Malmö General Hospital. The sex distribution was 831 women (63 per cent) and 493 men (37 per cent). The average age of the women was 65.6 ± 9.3 and of the men 63.4 ± 9.8. Seven hundred and ten right hips (54 per cent) were operated upon and 614 (46 per cent) on the left side. The types of prostheses used were in 695 cases (53 per cent) the Charnley, in 608 cases (46 per cent) the Lubinus or Brunswik, and in 21 cases (1 per cent) various other types. One hundred and six hips (8 per cent) were operated on for rheumatoid arthritis and 1,218 hips because of osteoarthritis and other reasons.

Ever since studies in our department showed that administration of dextran 70 led to a significant decrease in deep vein thrombosis following hip fractures (Ahlberg et al. 1968, Ahlberg 1969), this anti-thrombotic agent has been used consistently in every THR patient.

During the period 1969 to 1978, 500 ml of dextran 70 (Macrodex® 6 per cent in saline, Pharmacia AB, Sweden) was given intravenously during the operation and 500 ml on the second postoperative day. There has been no primary contraindication to this prevention as patients submitted to surgery have had their cardio-vascular status judged preoperatively.

Blood loss was substituted peroperatively and to a certain extent postoperatively. Postoperative management, including physiotherapy and full weight-bearing, was allowed on the first to third postoperative day.

Screening of deep vein thromboses by phlebography and pulmonary embolism by perfusion lung scan was performed during 1975–1977 in 135 patients.

Heparin given as treatment of thromboembolism was administered i.v. in a dose of 30,000 IU per 24 hours on four or six occasions. No regular tests were made of the effect upon the coagulation system.

In order to calculate the postoperative mortality we investigated every patient withdrawn from the population register within 3 months after the operation.

The actual case books, including autopsy charts and certificates of death, were picked out and scrutinized.

FPE was defined as pulmonary embolism which was the main cause of death.

One hundred patients, out of the 1,315 not exposed to FPE, were chosen at random to serve as a control group. Documents could be found in 94 per cent. Sex, operated side, weight, type of operating position, amount of bleeding and transfusion were recorded as well as the presence of acute chest pain in the postoperative period.

Data were compared using the multiple regression analysis and the chi-square method with Yate's correction.

RESULTS

Sixteen patients (1.2 per cent) died within 3 months postoperatively, the autopsy rate being 14/16. Nine patients had the diagnosis of FPE, which was verified by autopsy in 8 cases. This implies an incidence of 0.7 per cent. The mean time of postoperative survival for patients with FPE was 25 days. The other verified causes of death were bronchopneumonia in 3 cases, cardiac infarction in 2 and cardiac insufficiency in one case.

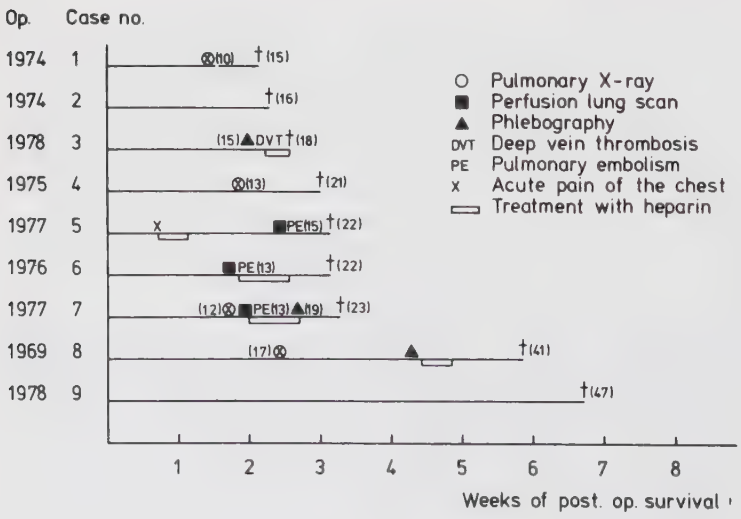

Figure 1. Patients with fatal pulmonary embolism.

Orthopaedic operations had previously been performed in 7 patients of the FPE group and in 32 of the control group. The difference is significant ($chi^2_{(1)} = 4.83$, $P < 0.05$). Two out of seven patients in the FPE group had had a previous THR. Five patients with FPE had a postoperative attack of acute chest pain compared with 8 in the control group ($chi^2_{(1)} = 10.92$, $P < 0.001$).

The patients with the diagnosis of FPE are listed in Figure 1. Seven patients died during the second and third week. Five patients had an attack of acute chest pain. Four of these patients had acute chest radiograms taken with negative results. Only one patient with chest pain (no. 5) received the clinical diagnosis of pulmonary embolism and was treated with heparin, which had to be stopped after 3 days because of a complicating haemorrhage. Pulmonary embolism was diagnosed in 3 patients (nos. 5, 6 and 7), who had been screened by perfusion lung scan. This test was positive for pulmonary embolism in every case. Two of these patients were treated for 5 days with intravenous injection of heparin. Patient no. 3 died during heparin treatment. The screening phlebography had shown bilateral thromboses of the vena profunda femoris. In patient no. 7, bilateral phlebography proved to be negative, but autopsy 5 days later showed thromboses on the non-operated side. Only one patient (no. 8) had clinical symptoms of deep vein thrombosis, which was verified by phlebography and found to be situated in the ilio-femoral vein on the operated side. This patient suffered from a hemiplegia, after 2 days of treatment, as a result of which heparin was abandoned. Autopsy was never performed. Patient no. 9 died in her home 5 days after leaving the hospital. No symptoms of thromboembolism were recorded.

Sex, operated side, type of prosthesis, bleeding per- or postoperatively, amount of blood transfusion, age, weight and number of operations in general, or gynaecological surgery in particular, did not differ significantly between the two groups.

There was no case of serious anaphylactic reaction (grade III–IV) or cardiac insufficiency recorded as a result of the administration of dextran 70.

Every patient with FPE had a completed prophylaxis with dextran.

DISCUSSION

Incidence figures of FPE after THR are relatively few. In a controlled study of 900 replacements of the hip, Crawford et al. (1968) found the incidence of FPE to be 1.8 per cent in the control series. This was to be compared with 0.9 per cent in the group with phenindione prophylaxis. However, the benefit was offset by three deaths from gastro-intestinal bleeding in the anticoagulation group. The autopsy rate was 87 per cent. Later, Charnley (1972) reported 1.4 per cent of FPE among early complications during the stay in hospital. In 1973, Coventry et al. reported two cases of FPE verified by autopsy in 58 patients without thromboembolic prevention (3.4 per cent). Johnson et al. (1977) have presented a fatality rate from pulmonary embolism of 2.3 per cent in 1,174 cases of THR without thromboembolic prophylaxis. Phenindione, intravenous heparin and dextran, all reduced the rate of FPE to 1.04 per cent in 7,959 hip arthroplasties. The autopsy rate was 88 per cent. Gruber et al. (1980) found in an international multicentre study, comparing dextran 70 and low-dose heparin, an overall frequency of 1.9 per cent with no statistical difference between the two groups. In a prospective and randomized study, Atik et al. (1970) reported one FPE in patients treated with dextran prophylaxis and 8 in the control group.

The relatively low incidence of FPE in our material (0.7 per cent) is possibly the result of our interest in diagnostic as well as screening procedures, including lung scan and phlebography, which may have contributed to the anticoagulative treatment of some presumptive cases of FPE.

Previous operations for orthopaedic reasons were more common in the group of FPE than in the controls. The reason might be that patients with previous deep vein thrombi have an increased risk of developing new thrombi and emboli. It must not be overlooked that the significant difference might be a result of repeated statistical evaluations. Orthopaedic operations

might also have been better documented than others in the orthopaedic case book.

According to Johnson et al. (1977), premonitory symptoms are very rare in FPE after THR. However, Bell et al. (1977) found in The Urokinase Pulmonary Embolism Trial that chest pain was present in 89 per cent of patients with clinically suspected pulmonary embolism verified by angiography. By scrutinizing the bedside reports in all cases, we found that acute attacks of chest pain had been noted in 5/9 cases. By comparing this rate with that of the control group we found that this premonitory symptom was significantly more common in FPE.

Thus, an acute attack of chest pain in the postoperative period must be taken seriously as being an indication of pulmonary embolism. A perfusion and ventilation lung scan should then be utilized as an objective, diagnostic method of excluding pulmonary embolism.

In 4 cases with acute chest pain, a chest radiogram was performed. The result was consistently negative and no further measures were taken. However, a negative chest radiogram should give rise to an even greater suspicion of pulmonary embolism (Harris et al. 1967, Evarts & Feil 1971). A perfusion and ventilation lung scan is then the only logical course of action, apart from an ECG, which is of immediate interest to exclude cardiac reasons. Stein's findings that there do not seem to be any changes in the ECG specific for pulmonary embolism (Stein et al. 1975) are in agreement with ours. We did not find any consistent changes in the ECG of the 9 patients with FPE.

Minor pulmonary embolism is often asymptomatic. In 3 cases with the diagnosis of pulmonary embolism a perfusion lung scan was performed as a screening procedure. As there are no data regarding the minimum size and number of emboli sufficient to cause death, every case of pulmonary embolism should be considered and treated (Gruber et al. 1977).

The time of onset of FPE in our material corresponds well with the noted maximal onset during the second and third week reported by Johnson et al. (1977) and Sevitt & Gallagher (1961).

Autopsy studies of FPE have shown that between half (Hume et al. 1970) and two-thirds of the cases (Havig 1977) show evidence of previous embolism.

A small pulmonary embolism can be the precursor of an eventual massive embolism, which has been reported to account for 80 per cent of FPE (Sevitt & Gallagher 1961).

Heparin treatment for 3–5 days did not prevent FPE in 3 patients. It is to be assumed that anticoagulative prevention must be extended for a longer period of time to allow the fibrinolytic system to resolve thrombi and emboli. The heparin treatment was not standardized in our study which explains the irregular duration of the treatment. We have now decided to extend the anticoagulative treatment to a period of 6 weeks. However, FPE can occur soon after the diagnosis of pulmonary embolism and the initiation of heparin treatment (patient no. 3).

Several reports have documented proximal thrombi in the ilio-femoral veins to be the main source of pulmonary embolism (Sevitt & Gallagher 1961, Havig 1977). Seventy-five per cent of FPE have been found to originate in the caval and ilio-femoral segment (Havig 1977). The two positive phlebographies in our material both had thrombi in the femoral vein. This location of deep vein thrombosis is common in patients after THR in contrast to patients undergoing general surgery (Nillius & Nylander 1979). To prevent, diagnose and treat these thrombi seems to be an all-important goal of thromboprophylaxis in THR.

In our study, FPE was the most common cause of death within 3 months after THR. Greater efforts seem to be necessary in order to assess the premonitory symptom of acute chest pain. A lung scan, as soon as possible, is recommended as the most simple and objective way of excluding pulmonary embolism. Treatment of pulmonary embolism should include anticoagulants for an adequate period of time.

CONCLUSIONS

1. The incidence of FPE was 0.7 per cent in 1,324 patients, all treated with dextran prophylaxis.

2. FPE was the most common cause of death within 3 months after THR.
3. Previous orthopaedic operations are a point to be noted concerning the possibility of developing FPE after THR.
4. Acute attacks of chest pain in the postoperative period are an important symptom, which should be followed by a lung scan in order to rule out pulmonary embolism.
5. Chest radiogram alone is inadequate for the evaluation of acute chest pain after THR.
6. Heparin therapy for a short period of time did not prevent FPE in cases with a scintigraphic diagnosis of pulmonary embolism.

REFERENCES

Ahlberg, Å., Nylander, G., Robertson, B., Cronberg, S. & Nilsson, I. M. (1968) Dextran in prophylaxis of thrombosis in fractures of the hip. *Acta Chir. Scand.,* Suppl. 387, 83–85.

Ahlberg, Å. (1969) *Trombosprofylax med Macrodex i ett collum-frakturmaterial.* Studentlitteratur, Lund, Sweden.

Atik, M., Harkess, J. W. & Wichman, H. (1970) Prevention of fatal pulmonary embolism. *Surg. Gynecol. Obstet.* **130**, 403–413.

Bell, W. R., Simon, T. L. & De Mets, D. L. (1977) The clinical feature of submassive and massive pulmonary emboli. *Am. J. Med.* **62**, 355–360.

Cavendish, M. E. & Charnley, J. (1972) *A review of the complications of low friction arthroplasty in the elderly.* Wrightington Int. Publication No. 37.

Charnley, J. (1972) Long term results of low friction arthroplasty of the hip as a primary procedure. *J. Bone Joint Surg.* **54**-B, 61–76.

Coventry, M. B., Nolan, D. R. & Beckenbaugh, R. D. (1973) "Delayed" prophylactic anticoagulation. A study of results and complications in 2012 total hip arthroplasties. *J. Bone Joint Surg.* **55**-A, 1487–1492.

Crawford, W. J., Hillman, F. & Charnley, J. (1968) *A clinical trial of prophylactic anticoagulant therapy in elective hip surgery.* Publication No. 14, Centre for Hip Surgery, Wrightington Hospital, Wiggan, England.

Donaldson, G. A., Williams, C., Scannell, J. G. & Shaw, R. S. (1963) A reappraisal of the application of the Trendelenburg operation to massive fatal embolism. Report of a successful pulmonary-artery thromboectomy using a cardio-pulmonary bypass. *N. Engl. J. Med.* **268**, 171–174.

Evarts, C. M. & Feil, E. J. (1971) Prevention of thromboembolic disease after elective surgery of the hip. *J. Bone Joint Surg.* **53**-A, 1271–1280.

Fitts, W. T., Jr., Lehr, H. B., Bitner, R. L. & Spelman, J. W. (1964) An analysis of 950 fatal injuries. *Surgery* **56**, 663–668.

Freiman, D. G., Suyemoto, J. & Wessler, S. (1965) Frequency of pulmonary thromboembolism in man. *N. Engl. J. Med.* **272**, 1278–1280.

Gruber, U. F., Duckert, F., Friedrich, R., Torhorst, J. & Rem, J. (1977) Prevention of postoperative thromboembolism by Dextran 40, low doses of Heparin, or Xantinol Nicotinate. *Lancet i*, 207–210.

Gruber, U. F., Saldeen, T., Brokop, T., Eklöf, B., Eriksson, I., Goldie, I., Gran, L., Hohl, M., Jonsson, T., Kristersson, S., Ljungström, K. G., Lund, T., Maarman Moe, H., Svensjö, E., Thomson, D., Torhorst, J., Trippestad, A. & Ulstein, M. (1980) Incidences of fatal postoperative pulmonary embolism after prophylaxis with dextran 70 and low-dose heparin: an International multicentre study. *Br. Med. J.* **1**, 69–72.

Harris, W. H., Salzman, E. W. & Desantis, R. W. (1967) The prevention of thromboembolic disease by prophylactic anticoagulation. *J. Bone Joint Surg.* **49**-A, 81–89.

Havig, Ö. (1977) Deep vein thrombosis and pulmonary embolism. *Acta Chir. Scand.,* Suppl. 478.

Hume, M., Sewitt, S. & Thomas, D. P. (1970) *Venous thrombosis and pulmonary embolism.* Harvard University Press, Cambridge, Massachusetts.

Johnson, R., Green, J. R. & Charnley, J. (1977) Pulmonary embolism and its prophylaxis following Charnley total hip replacements. *Clin. Orthop.* **127**, 123–132.

Kakkar, V. V. (1977) The prevention of acute pulmonary embolism. *Br. J. Hosp. Med.* **18**, 32–40.

Nillius, S. A. & Nylander, G. (1979) Deep vein thrombosis in total hip replacement. A clinical and phlebographical study. *Br. J. Surg.* **66**, 324–326.

Salzman, E. W. & Harris, W. H. (1976) Prevention of venous thromboembolism in orthopaedic patients. *J. Bone Joint Surg.* **58**-A, 903–912.

Sevitt, S. & Gallagher, N. G. (1961) Venous thrombosis and pulmonary embolism. A clinical-pathological study in injured and burned patients. *Br. J. Surg.* **48**, 475.

Stein, P. D., Dalen, J. E., McIntyre, K. M., Sasahara, A. A., Wenger, N. K. & Willis, P. W. (1975) The electrocardiogram in acute pulmonary embolism. *Prog. Cardiovasc. Dis.* **17**, 247–248.

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Scintigraphic Evaluation of Pulmonary Embolism After Total Hip Replacement, Using a Dry ^{99m}Tc-Microaerosol for Regional Ventilation

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Abstract. A new ^{99m}Tc-microaerosol was used for ventilation scintigraphy in combination with perfusion scintigraphy for studying the incidence of pulmonary embolism (PE) from 189 consecutive investigations in patients undergoing total hip replacement. Diagnostic criteria are presented. Perfusion defects of triangular shape were significantly more frequent in combination with ventilation mismatch (PE) than with ventilation match (not PE) ($P<0.001$). Re-evaluation of the scintigrams more than 2 months later gave identical results in more than 90% of patients and as regards the diagnosis of PE, in 93%. Attacks of sudden chest pain were more frequent in patients with pulmonary embolism ($P<0.01$), but measurement of arterial blood gases did not discriminate between patients with and without PE. The ^{99m}Tc-microaerosol provides a high resolution and images that are directly comparable to perfusion studies using the same, easily available isotope. In many aspects this new microaerosol seems to be superior to previously described radioaerosols and to ^{133}Xe for ventilation studies.

Introduction

An increased rate of pulmonary embolism (PE) has been reported in high-risk patients after major surgery such as total hip replacement (THR) (Harris et al. 1972; Charnley 1972; Coventry et al. 1973; Johnson et al. 1977; Dorr et al. 1979). The majority of these emboli are asymptomatic (Freiman et al. 1965; Hildner and Ormond 1967).

Previous studies of THR in our departments have demonstrated a frequency of PE in 22% of patients (Nillius et al. 1978). Furthermore, fatal PE was found to be the most common cause of post-operative mortality within 3 months (Fredin and Nillius 1982). The purpose of the present study was to make a scintigraphic evaluation of PE after THR using a dry ^{99m}Tc-microaerosol (Arborelius 1982) not previously applied in clinical practice. We also wanted to test the reproducibility of the scintigraphic evaluation and to investigate whether sudden chest pain or arterial hypoxia contributes to the diagnosis of PE.

Patients

The study was made after 200 operations on 190 patients, being the first part of a study concerning the prevention of thromboembolism in THR. Specific information was obtained pre-operatively from each patient concerning cardiovascular, pulmonary or other diseases.

A standardized procedure of THR was performed, mainly using the Charnley (91), the Lubinus (84) or other type of prosthesis (14). Free weight-bearing was allowed on post-operative day 1 or 2. Eleven patients were excluded from the study. They refused to take part or were discharged from the hospital before post-operative day 10. Of the remaining patients, 128 were women and 61 men. The mean age was 64 ± 13 years.

Twenty-three patients with a positive diagnosis of PE were randomly selected for a second perfusion test made after 1 week of heparin therapy to confirm the reversibility of the pulmonary artery occlusion.

Methods

Every patient had a lung scintigraphy performed on post-operative day 10–14. An AP and lateral chest radiogram was taken usually within 24 h prior to the scintigraphy. An ECG was always performed pre-operatively as well as a spirometry whenever any history of pulmonary disease was present. The scintigraphy was carried out with a scintillation camera (Radicamera II, General Electric) with a diverging collimator (low energy, 1,000 holes). Images were routinely obtained in the anterior, posterior, both lateral and the two posterior oblique positions and recorded on a black and white polaroid film (Polaroid Co., Cambridge, U.K.).

Perfusion scintigraphy was performed after an IV-injection of ^{99m}Tc-MAA in a dose of 70–100 MBq.

Ventilation scintigraphy was carried out by inhalation of 70–100 MBq ^{99m}Tc-labelled colloidal $Sn(OH)_3$, which formed when 0.5 mg $SnCl_2$, dissolved in 0.1 ml ethyl alcohol, was added to the pertechnetate solution. A modified jet nebulizer produced a primary aerosol with a size from 0.5 to 10 μ. Large fractions were impacted on a multiple stage cascade impactor and the water evaporated at 70 C resulting in a dry microaerosol with only a few particles larger than 0.5 μ. The half-life in the lungs was 4.5 h. Ninety-five per cent of the inhaled activity was located in the lung fields (Arborelius 1982). The inhalation time was 2 10 min and the time to collect 400 kcounts usually less than 1 min. The ventilation study was usually made 2 h after the perfusion study but postponed to the following day in single patients investigated in the afternoon. The

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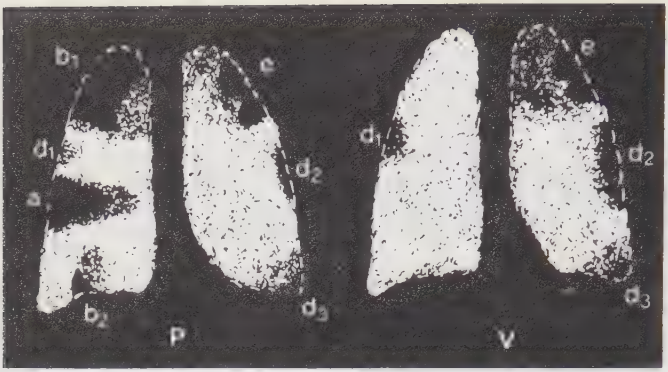

Fig. 1. Schematic representation of scintigraphic abnormalities. *P* perfusion scintigraphy; *V* ventilation scintigraphy. *a* Segmental and triangular perfusion defect. Complete loss of perfusion in at least one projection. b_1 Large, non-triangular perfusion defect. One point towards the hilum gives suspicion of embolus. b_2 Subsegmental, triangular perfusion defect. d_1 Small, peripheral perfusion decrease. Not complete loss of perfusion in any projection. d_2 Small, peripheral perfusion defect. Not triangular or extending towards the hilum in any projection. d_3 Small, peripheral perfusion defect and decrease. Allocated to group *e* if visible in more than one projection or if chest radiogram is completely normal in the same area. *e* Large, non-triangular perfusion defect. *a*, b_1 and b_2 demonstrate ventilation mismatch, all the others ventilation match

images were evaluated together with the chest radiograms by an experienced clinical physiologist to whom the type of prophylaxis was unknown.

In order to study the reproducibility of the scintigraphic interpretation, a second evaluation was made by M.A. 2 months after the first. He was not informed in advance. The scintigraphies were presented without names or other data. The observer had to register the images as normal or abnormal. The abnormalities had to be defined as a perfusion decrease or defect, segmental or non-segmental, with a definition of shape and position, as well as ventilation match or mismatch. Furthermore, he had to establish the final diagnosis, PE or not.

Arterial blood samples were taken by direct puncture of the radial artery before the scintigraphy for analyses of blood gases. Attacks of sudden chest pain were noted from the daily reports in the patients' records.

Definitions

1) Perfusion defect: No visible perfusion in major part of the area.

2) Perfusion decrease: Decreased but not absent perfusion in the area.

3) The diagnosis of PE was made according to the following criteria:

Positive: a) Patients without previous history of lung disease. Chest radiogram without signs of obstructive lung disease and with normal parenchyma in the area of the perfusion defect: One or several triangular perfusion defects involving at least one segment. Ventilation scintigraphy was not performed.

b) (1) Patients with history of, and/or chest radiogram giving suspicion of, lung disease, in which the perfusion defects – triangular or not – involved at least one segment and were substantially larger than the corresponding radiographic abnormality; or (2) patients and chest radiograms as in group *a* but with triangular perfusion defects involving at least the larger part of one segment. Normal ventilation of the non-perfused area (mismatch).

Negative: c) No perfusion abnormality.

d) Small, peripheral, non-triangular decreases or defects of perfusion.

e) Patients and defects as defined under *b*, but without ventilation of the non-perfused area (match).

Typical abnormalities as defined unter *a–e* are demonstrated in Fig. 1.

Every patient with a positive diagnosis of PE was treated with heparin injected IV during 1 week as well as warfarin for another 5 weeks.

The statistical analysis was made by the Student's *t*-test and the chi^2-test.

Results

The results of the scintigraphic evaluation are given in Table 1. The total incidence of PE was 20%.

A control scintigraphy after 1 week was obtained in 23 of 37 patients (62%) positive for PE. A partial or complete regression was noted in 22 patients. The defect that remained unchanged after 1 week had disappeared 6 months later. Four patients had another scintigram performed after a second THR. The earlier perfusion defects had disappeared in all but one, belonging to group *a*. In total, there was a scintigraphic reperfusion of the defect in 26 patients of 27 having a follow-up perfusion scintigraphy. There were

Table 1. Results of the evaluation (the letters correspond to the diagnostic criteria in the text)

	Total	Group	Number	1 week follow-up		Unchanged
				Complete regression	Partial regression	
Positive	37	a	9	2	3	1[a]
		b	28	10	7	
Negative	152	c	68			
		d	70			
		e	14			
Not performed	11					
Total	200					

[a] Reperfused 6 months later

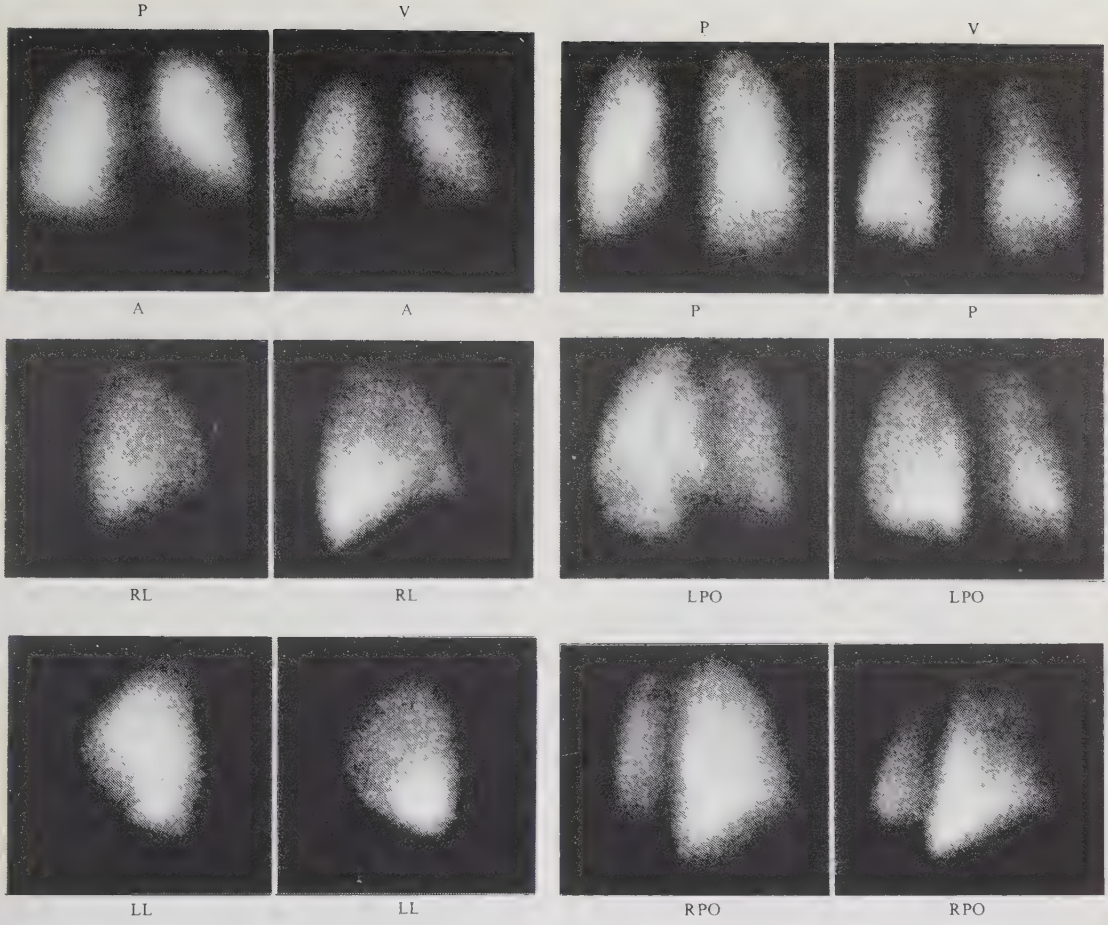

Fig. 2. Perfusion (*P*) and ventilation (*V*) scintigraphy. Projections Anterior (*A*), posterior (*P*), right lateral (*RL*), left lateral (*LL*), right posterior oblique (*RPO*), left posterior oblique (*LPO*). Triangular defect (h_2) in the left posterior oblique projection without a corresponding defect in the ventilation scintigraphy

Table 2. Blood gases related to PE (kPa)

Total[a]		N[b]	PaO_2	N[b]	$PaCO_2$
PE	39	23	10.3 ± 1.4	23	4.8 ± 0.4
PE >2 segments	13	13	9.7 ± 1.1	13	4.9 ± 0.4
Non-PE	150	81	10.2 ± 1.3	81	4.8 ± 0.5

[a] all patients
[b] number of blood samples obtained

no deaths due to PE. Ventilation scintigraphy was necessary for a positive or negative diagnosis in 42 patients (groups $b+e$). The perfusion defect suspected for PE, had a triangular shape with at least one point towards the hilum in 23 cases of 28 in group *b* and in 1 case of 14 in group *e*. This difference was significant ($P < 0.001$).

The second, blind re-evaluation of the scintigraphies was identical with the primary one in 92% of cases. There was a 93% agreement in the diagnosis of PE.

The blood gas tensions measured in 104 patients are presented in Table 2. No significant difference was found between patients with PE and those without, nor between patients with PE involving two segments or more and those without PE. A sudden attack of chest pain occurred in 15 of 189 patients (8%). Seven had scintigraphic signs of PE. There was a significant difference in sudden attacks of chest pain between patients with scintigraphic PE and those without ($P < 0.01$).

Discussion

This study differs from the majority of previous studies in the following aspects: (1) It is prospective and concerns a non-selected group of high-risk patients. The diagnostic criteria applied are founded on earlier studies of angiography (Gilday et al. 1972; McNeil 1976; Cheely et al. 1981; Goris and Daspit 1981; Rosenow et al. 1981). (2) The ventilation scintigraphy produced images directly comparable to the perfusion images in all six projections (Fig. 2).

The number of fatal PE, 0.7%–3.4% (Coventry et al. 1973; Fredin and Nillius 1982) is high enough to motivate an effort to diagnose and treat PE in the post-operative course. The majority of fatal PE has been reported to occur during the post-operative weeks 2–4 (Sevitt and Gallagher 1961; Johnson et al. 1977; Fredin and Nillius 1982). However, fatal pulmonary emboli are usually preceded by non-fatal ones (Freiman et al. 1965; Havig 1977). These may be discovered by screening scintigraphy.

The use of angiography, although more specific than pulmonary scintigraphy, was not considered possible in the present study, involving patients without clinical suspicion of PE. Therapy with anticoagulants is contraindicated before post-operative day 10 due to the risk of bleeding in the wound area. Therefore, screening before day 10 may give an early diagnosis but also provide a therapeutical problem.

Ventilation scintigraphy is considered useful for improving the specificity of the scintigraphic test (Pircher et al. 1965; Taplin and Poe 1965; McNeil 1976). With ^{133}Xe, a dose of approximately 700–1400 MBq has to be used, but due to difficulties with aerosol techniques it is still preferred by many. Only one projection is obtained. Many investigators rely on a single, dorsal projection (Biello et al. 1979; Cheely et al. 1981; Rosenow et al. 1981). Some improvement may be achieved by choosing the projection best visualizing the perfusion defect (McNeil 1976).

The low resolution of the ^{133}Xe image makes it difficult to interpret and to compare with the perfusion image. Perfusion defects smaller than one segment are especially difficult to register and would thereby increase the risk of false positive diagnosis of PE. This fact has been accepted as a reason for not performing ventilation scintigraphy, in up to 27% of the patients (McNeil 1976).Furthermore, a single dorsal projection of ^{133}Xe will hardly be informative when compared with perfusion defects seen in other projections. Relying on only the dorsal projection of the ventilation scintigraphy in our study, a positive diagnosis would have been uncertain in 12 patients of 28 in group *b*. Likewise, a confirmed negative diagnosis would have been false positive in two of eleven patients in group *e*.

For the reasons given above, we have found the ^{133}Xe ventilation scintigraphy to be inadequate. Ventilation studies with ^{81}Kr are directly comparable with ^{99m}Tc scintigraphies (Fazio and Jones 1975; Goris and Daspit 1981). However, the half-life of the ^{81}Rb mother is only 5 h which makes ^{81}Kr unavailable at our hospital.

When ^{81}Kr was used, fewer mismatch scintigraphies with negative angiographies were reported (Goris and Daspit 1981). A possible explanation is the high resolution of the ^{81}Kr. For the same reason, the microaerosol in our study can be supposed to provide few false positive diagnoses.

Aerosols of the soluble pertechnetate, rapidly disappear from the lung fields (Cook and Lander 1971). The consequence is an interfering activity in the airways and a low activity in the lung fields. Aerosols used in the valuable pioneer works by Pircher et al. (1965) and Taplin and Poe (1965) did settle significantly in the airways while 95% of our dry microaerosol was deposited in small airways or alveoli. Obstructive lung disease does not change this pattern (Arborelius 1982), while central deposition was a problem in earlier studies in patients with COAD (Chronic Obstructive Airway Disease) is one of many accepted abbreviations. However, it can be changed to: "... such disease"

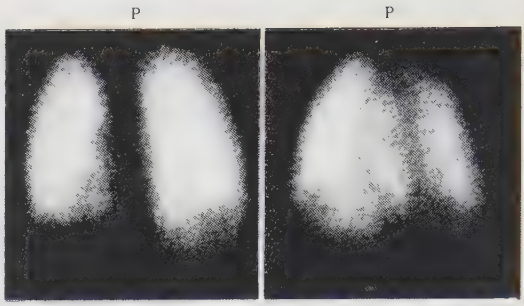

Fig. 3. Perfusion scintigraphy after 1 week of the same patient as in Fig. 2. Compare the diffuse shape of the defect (d_3) in the *LPO* projection with that of Fig. 2

A ventilation study can be made with microaerosols whenever the remaining activity from the perfusion study can be superseded twice by inhaled ^{99m}Tc. Of course, ^{113m}In-aerosol may be used for immediate inhalation scintigraphy (Isawa et al. 1971). However, the very hard radiation of this isotope renders scintigrams with poorer resolution and presents a radiation problem to the personnel. Furthermore, the cost of using another isotope is added.

The polaroid film registers an area as almost black if the true activity is, at maximum, 25% of the activity in areas read as completely white. The activity of the perfusion scintigraphy usually decreases to approximately 30% within 2 h. A later tripling of the activity over the lung fields during the ventilated study will not increase the residual activity of approximately 8% (30% × 25%) in a non-perfused/non-ventilated area (match). Thus, this area will still be registered as black. On the other hand, a non-perfused but ventilation area (mismatch) contains about 75% of the maximal activity and will therefore be registered almost as luminescent as those with maximal activity.

Multiple viewing has been advocated since 1967 (Sasahara et al. 1967). We used six projections in perfusion as well as in ventilation scintigraphy. Perfusion defects may be demonstrated in the two posterior oblique projections but not in the lateral ones, where the defects are covered by the activity of the normally perfused parenchyma (Fig. 2: P, LPO). Perfusion defects with a triangular shape, pointing at the hilum, were considered to indicate PE in this study. In patients with perfusion abnormalities of group *b* and *e*, triangular defects were significantly more common in group *b* (mismatch) than in group *e* (match). This difference supports the hypothesis that a perfusion defect of triangular shape indicates PE. With our criteria applied to the illustrations of Goris and Daspit (1981), patients without emboli would fall into our group *e* and those with emboli into group *a* and *b2*, respectively. According to our classification, their first illustration does show large, rounded perfusion defects, judged as segmental although not following segmental borders.

There was no perfusion abnormality in 68 patients (36%), group *c*. As the sensitivity of perfusion scintigraphy was close to 100% (Rosenow et al. 1981), a ventilation study was not considered necessary in these patients. Minor peripheral decreases or defects of perfusion occurred in 70

patients (37%), group *d*. There were insufficient facilities for ventilation scintigraphies in all patients at the time of the study. Also, the probability of minor defects corresponding to PE was considered less than 10% (Rosenow et al. 1981). Therefore, these changes were classified as negative even without a ventilation test.

The diagnosis PE was based on perfusion scintigraphy alone in 9 cases of 37 (24%), group *a*, where one or several segmental defects of triangular shape were found in patients with healthy lungs and a normal chest radiogram. Rosenow et al. (1981) reported a high probability (approximately 90%) of positive diagnoses for this type of defect. However, the 1-week follow-up demonstrated that typical defects, as in group *a* would be classified in group *d* after reperfusion (Fig. 3).

A ventilation scintigraphy would have increased the diagnostic accuracy and decreased the risk of a false positive diagnosis in group *a* and a false negative in group *d*. We now consider ventilation studies necessary and perform them in all patients with any perfusion abnormality. Perfusion defects which decreased or disappeared after 1 week of heparin treatment were considered as recent PE.

Regarding confirmed negative or positive diagnosis, match or mismatch, it seems illogical to deal with mixed groups (McNeil 1976; Goris and Daspit 1981; Cheely et al. 1981). A ventilation defect is either due to obstruction of the airways or to abnormal parenchyma. Both types provide secondary perfusion abnormalities (match) (Arborelius 1969). A primary perfusion defect is commonly caused by an embolus of venous origin. The ventilation is not affected (mismatch). Consequently, the diagnostic criteria for PE must be either positive (mismatch) or negative (match). If both patterns are registered, which may happen as embolism certainly occurs also in obstructive lung disease, a ventilated perfusion defect is most likely due to pulmonary embolism. Nevertheless, low probability for pulmonary embolism in mixed groups and with small defects has been claimed (Cheely et al. 1981; Goris and Daspit 1981). However, some groups in these studies were too small to allow statistical calculations. Cheely et al. (1981) had three patients with perfusion-ventilation (V/Q) mismatch in the subsegmental non-segmental group and only three in the lobar segmental group with V/Q match. Goris and Daspit (1981) had a total of four patients with mixed patterns and McNeil (1976) five patients. The size of the group having subsegmental defects is not clearly apparent from her protocol.

Using Bayes' theorem (McNeil et al. 1975), a calculation from the results of Cheely et al. (1981), Goris and Daspit (1981) as well as from McNeil (1976) renders a probability for PE of 0.93 for mismatch and 0.11 for match. Furthermore, methodological errors such as low resolution with ^{133}Xe may have provided unclear information, especially concerning subsegmental defects which may explain some of the false positive diagnoses reported by McNeil (1976). The delay of angiography can involve spontaneous lysis of a PE, which also may provide a false positive diagnosis (Goris and Daspit 1981).

The diagnostic reproducibility seems acceptable with the criteria applied in our study. A high reproducibility was also reported by Bateman et al. (1977), demonstrating an agreement with the final diagnosis of 86% when three observers evaluated perfusion-ventilation scintigraphies together with chest radiograms.

Blood gases were almost identical when comparing the groups with and without PE. Not even when selecting the major PE, equal to two or more segments, could a significant difference be found. We were unable to confirm the findings of Goodall and Greenfield (1980), pointing to a low arterial PO_2 in PE.

Goodall and Greenfield (1980) reported that pleuritic chest pain did not differ significantly between patients with positive and negative angiograms. Our findings are contradictory. Hurson et al. (1979) noted clinical symptoms in 35% of patients with scintigraphic PE. Chest pain in patients with clinically diagnosed PE was reported in 53%–89% (Bell et al. 1977).

Sudden chest pain in the post-operative course should raise a strong suspicion of PE and is a strong indication for scintigraphy together with a chest radiogram.

Conclusions

1. Ventilation scintigraphy with a dry ^{99m}Tc-microaerosol provides an improvement in clinical work by combining a scintigram of high quality with a short time of investigation. Six projections are easily obtained and the images are directly comparable with the perfusion images.

2. Ventilation scintigraphy of every perfusion defect or decrease will increase the diagnostic accuracy.

3. A perfusion defect of triangular shape, pointing towards the hilum, appears to indicate PE.

4. Decrease of a perfusion defect within 1 week supports the diagnosis of a recent embolus and indicates prolonged therapy with anticoagulants.

5. Sudden chest pain in the post-operative course seems to be a strong indication for a pulmonary scintigraphy together with a chest radiogram.

6. Arterial blood gases are not useful for screening patients with suspected PE.

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References

Arborelius Jr M (1969) Influence of unilateral hypoventilation on distribution of pulmonary blood flow in man. J Appl Physiol 26:101–104

Arborelius Jr M (1982) Generation of a microaerosol suitable for deposition in the peripheral airways. In: Inhalation therapy in the management of airway obstruction. Eur J Respir Dis 63:Suppl 119:19–27

Bateman NT, Coakley AJ, Croft DN, Lyall JRW (1977) Ventilation-perfusion lung scans for pulmonary emboli. Accuracy of reporting. Eur J Nucl Med 2:201–203

Bell WR, Simon TL, DeMets DL (1977) The clinical features of submassive and massive pulmonary emboli. Am J Med 62:355–360

Biello DR, Matter AG, McKnight RC, Siegel BA (1979) Ventilation-perfusion studies in suspected pulmonary embolism. AJR 133:1033–1037

Charnley J (1972) The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. J Bone Joint Surg (Am) 54B:61–76

Cheely R, McCartney WH, Perry JR, Delany DJ, Bustad L, Wynia VH, Griggs TR (1981) The role of noninvasive tests versus pulmonary angiography in the diagnosis of pulmonary embolism. Am J Med 70:17–22

Cook DJ, Lander H (1971) Inhalation pulmonary scintiphotography using pertechnetate. AJR 113:682–689

Coventry MB, Nolan DR, Beckenbaugh R (1973) "Delayed" prophylactic anticoagulation: A study of results and complications in 2,012 total hip arthroplasties. J Bone Joint Surg (Am) 55A:1487–1492

Dorr LD, Sakimura I, Mohler JG (1979) Pulmonary emboli following total hip arthroplasty: Incidence study. J Bone Joint Surg (Am) 61A:1083-1087

Fazio F, Jones T (1975) Assessment of regional ventilation by continuous inhalation of radioactive Krypton-81m. Br Med J 3:673–676

Fredin HO, Nillius AS (1982) Fatal pulmonary embolism after total hip replacement. Acta Orthop Scand, Acta Orth Scand 53:407–412

Freiman DG, Suyemoto J, Wessler S (1965) Frequency of pulmonary thromboembolism in man. N Engl J Med 272:1278–1280

Gilday DL, Poulose KP, DeLand FH (1972) Accuracy of detection of pulmonary embolism by lung scanning correlated with pulmonary angiography. AJR 115:732–738

Goodall RJR, Greenfield LJ (1980) Clinical correlations in the diagnosis of pulmonary embolism. Ann Surg 191:219–223

Goris ML, Daspit SG (1981) Krypton-81m ventilation scintigraphy for the diagnosis of pulmonary emboli. Clin Nucl Med 6:207–212

Harris WH, Salzman EW, DeSanctis RW, Coutts RD (1972) Prevention of venous thromboembolism following total hip replacement. Warfarin vs dextran 40. JAMA 220:1319–1322

Havig Ö (1977) Deep vein thrombosis and pulmonary embolism. Acta Chir Scand (Suppl) 478

Hildner FJ, Ormond RS (1967) Accuracy of the clinical diagnosis of pulmonary embolism. JAMA 202:567–570

Hurson B, Ennis JT, Corrigan TP, MacAuley P (1979) Dextran prophylaxis in total hip replacement: A scintigraphic evaluation of the incidence of deep vein thrombosis and pulmonary embolus. Ir J Med Sci 148:140–144

Isawa T, Hayes M, Taplin GV (1971) Radioaerosol inhalation lung scanning: its role in suspected pulmonary embolism. JNM 12:606–609

Johnson R, Green JR, Charnley J (1977) Pulmonary embolism and its prophylaxis following the Charnley total hip replacement. Clin Orthop 127:123–132

McNeil BJ (1976) A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism. JNM 17:613–616

McNeil BJ, Keeler E, Adelstein SJ (1975) Primer on certain elements of medical decision making. N Engl J Med 293:211–215

Nillius SA, Arborelius Jr M, Nylander G (1978) Pulmonary embolism in total hip replacement. A clinical study using ^{99m}Tc perfusion lung scan. Thesis, University of Lund, pp 53–69

Pircher FJ, Temple JR, Kirsch WJ, Reeves RJ (1965) Distribution of pulmonary ventilation determined by radioisotope scanning. AJR 94:739–746

Rosenow III EC, Osmundson PJ, Brown ML (1981) Pulmonary embolism. Mayo Clin Proc 56:161–178

Sasahara AA, Belko JS, Simpson RG (1967) Multiple-view lung scanning. JNM 9:187–191

Sevitt S, Gallagher N (1961) Venous thrombosis and pulmonary embolism. A clinico-pathological study in injured and burned patients. Br J Surg 48:475–489

Taplin GV, Poe ND (1965) A dual lung scanning technique for evaluation of pulmonary function. Radiology 85:365–368

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SCREENING AND TREATMENT OF PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

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The effect of anticoagulative treatment of pulmonary embolism was studied in 63 patients out of 348 operated on with total hip replacement. Screening diagnosis of pulmonary embolism was obtained from ^{99m}Tc perfusion scintigraphy in combination with ^{99m}Tc-microaerosol ventilation scintigraphy and chest radiogram. The administration of heparin and warfarin was associated with hemorrhagic side effects in 7 per cent. The final outcome of surgery, however, was not interfered with. Fatal pulmonary embolism occurred in one patient (0.3 per cent) in whom the diagnosis had been missed.

Key words: dextran 70; heparin; hip replacement; pulmonary embolism; radionuclide imaging; warfarin

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Pulmonary embolism (PE) constitutes the main cause of death following total hip replacement (THR) (Coventry et al. 1973, Johnson et al. 1977, Fredin & Nillius 1982). Frequencies of PE up to 11 per cent have been reported when based on physical examination alone (Hurson et al. 1979), and up to about 20 per cent when using pulmonary scintigraphy (Nillius et al. 1978, Fredin & Arborelius 1982). The mortality of untreated PE varies between 30 per cent and 50 per cent (Morrell et al. 1963, Pollak et al. 1973). Death from PE may occur in spite of heparin treatment (Fredin & Nillius 1982). However, few reports are available.

The aim of the present investigation was to study the effect of and the complications of treatment of PE after THR as diagnosed by screening scintigraphy.

MATERIAL AND METHODS

A total of 348 patients were operated on with THR, 321 patients with primary operations and 27 with revision arthroplasties. There were 114 men and 234 women with an average age of 65 ± 10 years. Patients with rheumatoid arthritis were excluded. A standardized procedure of THR was performed using either the Charnley or the Lubinus prosthesis. The thromboembolic prevention was randomly allocated between two groups.

One group was given dextran 70 (Macrodex®). The doses were 1000 ml on the day of the operation and 500 ml on the first and third postoperative days, respectively. If the peroperative blood loss exceeded 2000 ml, another 500 ml of dextran 70 was added on the second day. Before the initial infusion of dextran 70, 10 ml of monovalent haptendextran (15 per cent dextran 1, molecular weight 1000 dalton, Pharmacia AB, Sweden) was injected i.v. (Messmer et al. 1980).

The other group was given a fixed combination of 5000 IU of sodium heparin and 0.5 mg dihydroergotamine mesylate (Orstanorm®) (HDHE). The dose was given subcutaneously every 12 h during 10 days starting 1–2 h prior to surgery. The combination was approved by the Pharmaceutical Department of the National Social Welfare Board.

Weight-bearing was allowed on the first or second post-operative day.

A pulmonary scintigraphy was performed on 324 patients using ^{99m}Tc-perfusion scintigraphy 10–14 days after surgery (Fredin & Arborelius 1982). In 24 patients scintigraphy could not be performed for various reasons such as discharge from hospital before the 10th day or refusal to participate.

In 36 unselected patients with PE, a second perfusion scintigraphy was carried out after 1 week of heparin treatment in order to study the re-perfusion of the scintigraphic defect, in the remaining 27 this procedure was omitted. Four of the latter had a second THR performed on a later occasion. At that time there were no remaining scintigraphic perfusion defects.

The treatment with heparin and warfarin was started immediately after a positive scintigraphic diagnosis was obtained. Sodium heparin was given i.v. in a dose of 7500 IU six times a day. The dose was reduced to 5000 IU in patients over the age of 70, or weighing less than 60 kg.

The heparin treatment was discontinued when the prothrombin complex (P&P) measured with Simplastin A (Warner & Chilcott, USA) had reached a therapeutic level – ≤ 25 per cent – following peroral administration of warfarin. A daily dose of 12.5, 10 and 7.5 mg warfarin was given the first 3 days, in all patients with a P&P > 90 per cent. The P&P was measured once a week after a steady state had been attained. The warfarin treatment ended after 6 weeks.

Five patients with PE were not given anticoagulative therapy. One patient with a gastric ulcer and liver dysfunction received dextran 40 (Rheomacrodex®), 500 ml daily for 5 days. Initial misinterpretation in the scintigraphic procedure was the cause in four cases.

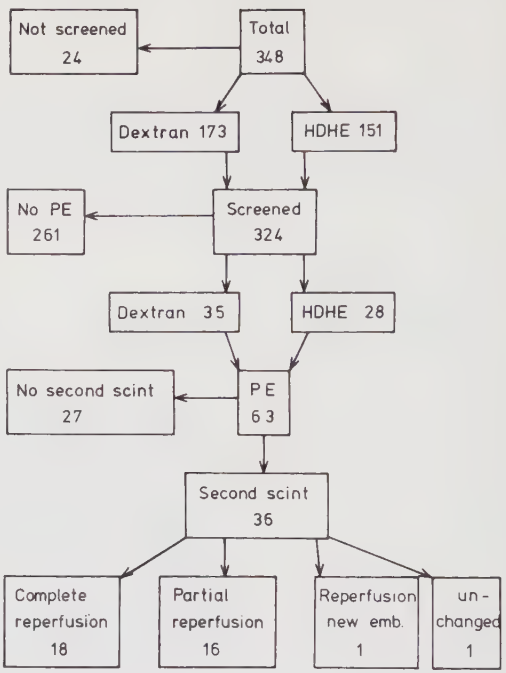

Figure 1. Flow scheme of patients with their thromboprophylaxis, screening and treatment for pulmonary embolism.

RESULTS

PE was diagnosed in 63 patients, 28 in the HDHE group and 35 in the dextran group (Figure 1). In all instances the diagnosis was based on the scintigraphy. Symptoms of PE prior to the scintigraphy were not observed.

Four of the 58 patients with anticoagulative treatment had complications during heparin and one during warfarin administration. One patient with multi-segmental emboli had several episodes of hemoptysis after 3 days on heparin and 12 days postoperatively. Three patients had a wound hematoma, one of these draining but with an uncomplicated healing of the wound. One patient had a subcutaneous hemorrhage following venous puncture after 9 days on warfarin.

The follow-up perfusion scintigraphy after 1 week of heparin administration, demonstrated a complete re-perfusion in 18 patients and a partial regression in 17 patients out of 36. In one of the 17 patients, re-perfusion was well as signs of new embolism were found. In another patient there was an unchanged perfusion image.

A follow-up scintigraphy was made in two patients among the five never treated with heparin or warfarin. One demonstrated a complete regression of the primary perfusion defect and the other a partial re-perfusion at the 1-week follow-up test.

The hospitalization period was prolonged until a steady state of P&P had been attained, on the average 5 days (range 4–19 days). The hemorrhagic complications in five patients delayed the discharge by on the average 6 days (range 2–19). The anticoagulant treatment with its complications added on the average 0.9 days of hospitalization, all patients included.

The mortality within 3 months after surgery was four patients out of 348, three of whom had

autopsy. In the fourth patient the clinical cause of death was cardiac infarction. This diagnosis was supported by laboratory signs and repeated electrocardiographic findings. In the autopsy cases the diagnosis was cardiac infarction in one case and septicemia following cholecystitis in another. One patient, however, died from pulmonary embolism:

A 73-year-old woman had DVT and PE found in routine phlebography and scintigraphy after her primary arthroplasty. Four years later she had her second hip arthroplasty performed. Low dose heparin in combination with dihydroergotamine was given as thromboprophylaxis for 10 days. The patient refused to participate in the screening phlebography of the operated leg but there were no signs or symptoms of DVT at any time. On the 13th postoperative day she had an episode of vertigo with sweating and palpitations interpreted as a relapse of atrial fibrillation previously verified by ECG. On day 14 there was dyspnea and coughing with a negative chest radiogram. On the suspicion of PE, heparin therapy was started but discontinued on the following day, since perfusion scintigraphy demonstrated only a slight defect atypical of PE and as 1 day later the ventilation scintigraphy did not support the diagnosis. Three weeks postoperatively a chest radiogram revealed pleura exudate, interpreted as due to cardiac failure. The following night she had an episode of pain in the back of her chest. Four weeks postoperatively, there was cardiac arrest and death. At autopsy, fresh emboli in the main trunks of the pulmonary artery were demonstrated as well as a major thrombosis in the femoral vein of the operated side.

DISCUSSION

Patients undergoing total hip replacement are at high risk of developing thromboembolism. Previous orthopaedic surgery has been reported to add further to the risk of fatal PE (Fredin & Nillius 1982), which is, on the whole, the most common cause of fatal outcome in the postoperative period. Reliable methods have been developed for the diagnosis of DVT as well as PE. These diagnostic efforts should, logically, result in anticoagulative therapy. However, this treatment may cause bleeding complications which could be disastrous in endoprosthesis surgery.

Treatment of PE with heparin and warfarin should be regarded as an extended prophylaxis against an enlargement of the PE and against further emboli. The purpose of anticoagulative treatment is also to prevent growth of existing DVT and the development of a post-thrombotic syndrome. The effect of heparin is to prevent thrombotic growth, while the natural fibrinolysis is active (Oakley 1968, Secker-Walker et al. 1970). However, it has also been reported that heparin may relieve the bronchial spasm by preventing the release of vasoactive amines from platelets in the embolus (Thomas 1965). Studies in dogs by Moser et al. (1973) indicated an enhancement of the embolic disintegration during heparin treatment by preventing accretion of fibrin-platelet layers on the surface of the embolus. Untreated patients demonstrated scintigraphic improvement less often and had more new perfusion defects than patients treated with anticoagulants (Secker-Walker et al. 1970).

Continuous administration of heparin provides a lower blood concentration and decreases the risk of bleeding complications (Salzman et al. 1975, Glazier & Crowell 1976). Intermittent administration, however, has recently been reported to prevent new PE (Wilson et al. 1981). There are also good reasons for adjusting the heparin dose to age and body weight (Salzman et al. 1975).

The complications to treatment with anticoagulants in the present study were almost exclusively due to heparin. However, no major disadvantage such as infection or delayed healing of the wound did occur as a result of the anticoagulative therapy.

We have considered the scintigraphic regression of the perfusion defect as a sign of recent PE. However, the PE might have resolved without heparin therapy as actually occurred in one of the patients studied.

Fatal PE is by some considered a rare event. The real incidence can be calculated only from autopsy data which must include every patient deceased within the first months after surgery. The clinical diagnosis is inadequate. Fatal PE is often asymptomatic and may therefore be mistaken for cardiac failure. The only patient with a fatal PE in this study demonstrates the fact that screening scintigraphy must be repeated if new symptoms or signs develop. As previously reported (Fredin & Nillius 1982), PE may recur in

spite of anticoagulative treatment – this was observed in one case in this study.

The selection of patients for treatment was entirely based on the screening scintigraphy, which is a simple and non-invasive but a less specific method than pulmonary angiography (Fredin & Arborelius 1982). Some smaller PE may have escaped detection. The outcome should be considered with this background.

Only 1/348 patients in this study died from fatal PE. This patient had not received proper treatment. The fatality rate is less but not significantly decreased as compared with earlier observations in our department (Fredin & Nillius 1982). Several thousands of observations would be needed to demonstrate significant differences in fatal PE.

This study demonstrates, however, that heparin – warfarin treatment may be used without serious side effects and with an investment of only one additional day of hospitalization on average.

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REFERENCES

Bell, W. R., Simon, T. L. & DeMets, D. L. (1977) The clinical features of submassive and massive pulmonary emboli. *Am. J. Med.* **62**, 355–360.

Coventry, M. B., Nolan, D. R. & Beckenbaugh, R. D. (1973) "Delayed" prophylactic anticoagulation: A study of results and complications in 2,012 total hip arthroplasties. *J. Bone Joint Surg.* **55**-A, 1487–1492.

Fredin, H. O. & Arborelius, M., Jr. (1982) Scintigraphic evaluation of pulmonary embolism after total hip replacement using a dry ^{99m}Tc-microaerosol for regional ventilation. *Eur. J. Nucl. Med.*, **7**, 494–499.

Fredin, H. O. & Nillius, S. A. (1982) Fatal pulmonary embolism after total hip replacement. *Acta Orthop. Scand.* **53**, 407–411.

Glazier, R. L. & Crowell, E. B. (1976) Randomized prospective trial of continuous versus intermittent heparin therapy. *J. Am. Med. Assoc.* **236**, 1365–1367.

Hurson, B., Ennis, J. T., Corrigan, T. P. & MacAuley, P. (1979) Dextran prophylaxis in total hip replacement: A scintigraphic evaluation of the incidence of deep vein thrombosis and pulmonary embolus. *Ir. J. Med. Sci.* **148**, 140–144.

Johnson, R., Green, J. R. & Charnley, J. (1977) Pulmonary embolism and its prophylaxis following the Charnley total hip replacement. *Clin. Orthop.* **127**, 123–132.

McIntyre, I. M. C. & Ruckley, C. V. (1974) Pulmonary embolism. A clinical and autopsy study. *Scott. Med. J.* **19**, 20–25.

Messmer, K., Ljungström, K. G., Gruber, U. F., Richter, W. & Hedin, H. (1980) Prevention of dextran-induced anaphylactoid reactions by hapten inhibition. Letter to the Editor. *Lancet* **1**, 975.

Morrell, M. T., Truelove, S. C. & Barr, A. (1963) Pulmonary embolism. *Br. Med. J.* **2**, 830–835.

Moser, K. M., Guisan, M., Bartimmo, E. E., Longo, A. M., Harsanyi, P. G. & Chiorazzi, N. (1973) In vivo and post mortem dissolution rates of pulmonary embolism and venous thrombi in the dog. *Circulation* **48**, 170–178.

Moses, D. C., Silver, T. M. & Bookstein, J. J. (1974) The complementary roles of chest radiography, lung scanning and selective pulmonary angiography in the diagnosis of pulmonary embolism. *Circulation* **49**, 179–188.

Nillius, S. A., Arborelius, M., Jr. & Nylander, G. (1978) On thromboembolism after total hip replacement, pp. 53–69. Thesis, University of Lund, Sweden.

Oakley, C. M. (1968) Conservative management of pulmonary embolism. *Br. J. Surg.* **55**, 801–805.

Pollak, E. W., Sparks, F. C. & Barker, W. F. (1973) Pulmonary embolism. *Arch. Surg.* **107**, 66–68.

Salzman, E. W., Deykin, D. & Shapiro, R. M. (1975) Management of heparin therapy: A controlled prospective trial. *N. Engl. J. Med.* **292**, 1046–1050.

Secker-Walker, R. H., Jackson, J. A. & Goodwin, J. (1970) Resolution of pulmonary embolism. *Br. Med. J.* **4**, 135–139.

Thomas, D. P. (1965) Treatment of pulmonary embolic disease. A critical review of some aspects of current therapy. *N. Engl. J. Med.* **273**, 885–892.

Wilson, J. E., III, Bynum, L. J. & Parkey, R. W. (1981) Heparin therapy in venous thromboembolism. *Am. J. Med.* **70**, 808–816.

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SCINTIGRAPHY AND CHEST RADIOGRAPHY IN SCREENING OF PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

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Running title: Pulmonary embolism in total hip replacement.

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ABSTRACT

Two hundred and ten patients were screened for pulmonary embolism after total hip replacement with chest radiography and perfusion-ventilation scintigraphy using a new, dry ^{99m}Tc-microaerosol and a detailed system for coding scintigraphic abnormalities. Chest radiography did not contribute significantly to the diagnosis of pulmonary embolism. In spite of a careful evaluation there are several possibilities of a false negative and a false positive scintigraphic diagnosis of PE.

KEYWORDS

Chest radiography; hip replacement; pulmonary embolism; radionuclide imaging.

INTRODUCTION

Patients operated upon with total hip replacement (THR) are at high risk of developing postoperative thromboembolic complications. Findings compatible with pulmonary embolism (PE) were scintigraphically registered in about 20 % (1,2) in previous works at our hospital. In one of the studies (2), a new, dry ^{99m}Tc-microaerosol (3) was used for ventilation scintigraphy in the diagnostic evaluation of perfusion abnormalities. Fatal PE was also found to be the most common cause of postoperative death within three months (4).

The purpose of the present study was to test a more detailed system for coding abnormalities in perfusion and ventilation scintigraphies and to evaluate the role of chest radiography in screening for PE.

MATERIAL AND METHODS

Two hundred and fifty-four consecutive patients were operated on with THR from November 1980 to May 1982, mainly using the Lubinus or the Charnley procedures. Forty-four patients did not participate in the study. The reasons were either refusal to take part or an incomplete postoperative follow-up. The non-participating group did not differ significantly from the remaining population concerning age, sex or type of prothesis. The two hundred and ten patients left for analysis had a mean age of 67 $\pm$ 11 years. One hundred and thirty-two were women (63 %) and seventy-eight were men (37 %).

The patients were investigated 10-14 days postoperatively with a perfusion scintigraphy, using an I.V. injection of 70-100 Mbq of ^{99m}Tc-MAA. In patients with perfusion abnormalities other than small peripheral areas of decreased perfusion (Fig. 1, code h), a ventilation scintigraphy was performed using inhalation of a dry ^{99m}Tc-microaerosol (2). The type, site and extension of the perfusion defects were recorded and compared with the outcome of the ventilation scintigraphy. All scintigrams were classified by an experienced clinical physiologist according to Fig. 1.

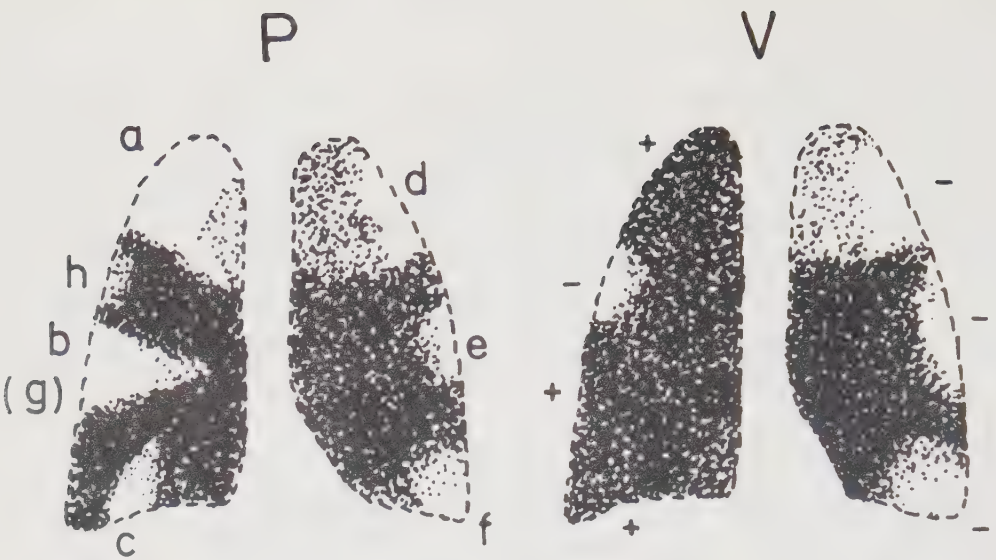

Fig. 1. System for coding of scintigraphic abnormalities.
Defect : No radioactivity visible;
Decrease : Obvious decrease but no complete loss of radioactivity.

Perfusion scintigraphy

a : A defect larger than one segment following segmental borders and pointing towards hilum or mediastinum.

b : A triangular segmental defect pointing towards hilum.

c : A triangular subsegmental defect pointing towards hilum.

d : A defect larger than one segment with a rounded border towards hilum.

e : A peripheral defect with a rounded border towards hilum not always following segmental borders.

f : A defect at the costodiaphragmal angle with a diffuse border towards the parenchyma.

g : A segmental or larger decrease as type a or b with obvious activity out to the peripheral lung border.

h : A small, peripheral decrease.

0 : No visible decrease or defect.

Ventilation scintigraphy

+ : Activity normal or obviously higher as compared with the perfusion activity in the same area.

- : Activity absent or lower than the corresponding perfusion activity in the same area.

The scintigraphic findings were evaluated as follows:

I. Perfusion code a - g : PE suspected:

(a) in combination with ventilation code + : diagnostic of PE, "PE +" (mismatch);

(b) in combination with ventilation code - : not diagnostic of PE, "PE -" (match).

II. Perfusion code h and 0 : No suspicion of PE, "PE 0".

Chest radiography in the PA and lateral position was made pre- and postoperatively prior to the scintigraphy. The radiograms were examined by an experienced radiologist who classified the site and type of abnormalities according to Table II and without knowledge of the scintigraphic findings. The scintigraphic and radiographic findings were then compared.

RESULTS

Chest radiography was performed on the average 13 $\pm$ 3 days (m $\pm$ SD) postoperatively and scintigraphy 14 $\pm$ 3 days.

The results of the scintigraphic evaluation are presented in Table I.

TABLE I

Evaluation of scintigraphic changes

PE + = changes diagnostic of pulmonary embolism (mismatch);
PE - = changes not diagnostic of pulmonary embolism (match);
PE 0 = no suspicion of PE.

Perfusion code	Ventilation code +	%	Ventilation code -	Total number
a	8	(89)	1	9
b	9	(69)	4	13
c	5	(71)	2	7
d	5	(23)	16	21
e	13	(33)	27	40
f	1	(13)	7	8
g	0		5	5
0, h				107
	41 (PE +)		62 (PE -)	210

A diagnosis of PE was made in 41 of the 210 patients (20 %), whereas in 62 patients (30 %) the scintigraphy was evaluated as "PE -". One hundred and seven scintigraphies were classified as code 0 or h (PE 0). Major perfusion changes as in code a and b had a normal ventilation (= PE +) in 17/22, whereas those of code d had a normal ventilation in 5/21.

The radiological changes are presented in Table II.

TABLE II

Classification of radiological changes

	No. of findings	
Pulmonary embolism without hemorrhage or infarction		
Indirect signs		
A. Ipsilateral elevation of the diaphragm	9	
B. Pleural fluid	1	
C. Lamellar atelectasis	23	
D. Dilatation of hilar arteries	2	
E. Acute cor pulmonale	0	
Direct signs		
F. Local or diffuse oligemia - Westermark´s sign	2	
G. Ipsilateral dilatation of the hilar artery - knuckle sign	2	
H. Reduction of vessel diameter distally to the occlusion	0	
Pulmonary embolism with hemorrhage		
I. Light/multiple infiltrates	2	
Pulmonary embolism with infarction		
J. Parenchymal defect close to the pleura, often connected with pleural fluid - Hampton´s hump	1	42 (37 patients*)
Old changes		
K. Emphysema		
L. Local fibrosis		
M. Signs of former operative procedures		
N. Relaxation of diaphragm/hernia		
O. Other findings		42
Normal chest radiograms		131
		215
*) Five patients in groups A-J had double findings		(210 patients)

Thirty-seven patients (18 %) (groups A to J) presented in all 42 signs compatible with PE and 42 patients (20 %) had stationary abnormalities considered as caused by previous lung disease (groups K to O). One hundred and thirty-one radiograms were regarded as normal.

The relationship between the scintigraphic and radiological findings can be studied in Table III.

TABLE III

Relationship between findings giving suspicion of pulmonary embolism in scintigraphy and radiography

PE + = changes diagnostic of pulmonary embolism (mismatch);

Scintigraphy: PE − = changes not diagnostic of pulmonary embolism (match);

PE 0 = no suspicion of PE.

Chest radiography: PE + = changes indicating PE.

		RADIOGRAPHY			
		PE +	Old changes	Normal	Total
SCINTIGRAPHY	PE +	8	10	23	41
	PE −	11	12	39	62
	PE 0	18	20	69	107
	Total	37	42	131	210

Thirty-seven patients had radiographic findings indicating PE. Eight of these had scintigraphic changes diagnostic of PE, 11 scintigraphic findings classified as "PE -" and 18 a scintigraphy evaluated as "PE 0". In 7 out of the 8 patients with "PE +", the radiographic findings, such as atelectases and elevation of the diaphragm, corresponded to ipsilateral scintigraphic abnormalities. Four out of the 11 patients with scintigraphic "PE -" had ipsilateral radiographic signs. Finally, 12 of the 18 patients in group "PE 0" had radiographic findings in the lower parts of the lungs with corresponding small scintigraphic abnormalities (code h) in the same area. The remaining 6 patients of the 18 had a normal perfusion scintigraphy (code 0).

Twelve patients had old changes in the radiograms and a scintigraphy evaluated as "PE -"; 6 of them had ipsilateral radiographic and scintigraphic findings.

Among 131 patients with a normal chest radiography, 23 had scintigraphic findings evaluated as "PE +".

Twenty-one major perfusion defects code a, b and d were diagnosed among 62 patients with scintigraphies evaluated as "PE -". Four of them had radiographic findings compatible with PE, 6 old radiographic changes and 11 a normal radiogram.

DISCUSSION

The scintigrams were made on the average two weeks postoperatively, which is before the period when most fatal emboli occur (4). The incidence of PE in the present study (20 %) is about the same as previously reported after THR using a less detailed classification of scintigraphic defects and an inconstant addition of ventilation scintigraphy in the evaluation of perfusion abnormalities (2).

The classification of scintigraphic changes are mainly founded on earlier studies comparing pulmonary angiography and scintigraphy (5-9). In these works, the probability for PE was considered high for large defects, code a and b, decreasing with the following code letters down to just above zero for code 0. Perfusion defects such as code e and f

were considered to represent areas of reperfusion. This conclusion was drawn from a one-week follow-up in an earlier study (2).

Some of the minor perfusion defects in the present study, code e and f, were evaluated as compatible with PE in 14/48 (29 %). In our previous study these changes were considered negative for PE and not ventilated (2), thereby probably providing a false negative diagnosis in some patients.

In spite of six scintigraphic projections, a perfusion defect may be evaluated as a perfusion decrease due to overlying parenchyma (e.g. code b versus code g and code e versus code h). Code h may also represent multiple, small emboli difficult to diagnose as match or mismatch even with an additional ventilation scintigraphy. A partially occluding embolus may not significantly decrease the perfusion, thereby escaping detection. These are other possible reasons for a false negative diagnosis of PE.

Twenty-one out of 62 patients had major perfusion defects, code a, b and d, with corresponding abnormal ventilation classifying them as PE -. Thus, it is obvious that even a large perfusion defect must be evaluated together with a ventilation scintigraphy in order to avoid a false positive diagnosis of PE.

Perfusion defects of a triangular form (code a, b and c), however, were combined with a higher frequency of ventilation scintigraphy (code +) than other types of defects and decreases (Table I).

Abnormalities in the chest radiograms of patients with PE are common (10) but considered non-specific (11). However, these changes are reported to be especially common in patients with cardiovascular disease which in our study was present in a minority of the patients. We found lamellar atelectasis to be the most frequent indirect sign of PE (5/41 - 12 %) as compared with a frequency of 11/41 - 27 % - in a study by Moses et al. (12). In their report, as in most of the others referred to, the selection of patients was made from clinical symptoms and signs of PE, whereas the patients in our study were postoperatively screened. This may explain our comparatively low frequency of radio-

logical findings, 8/41 (20 %), as compared to the findings of 38/41 (93 %) in patients with angiographically documented acute pulmonary embolism (12).

The time interval between the scintigraphy and the chest radiography was short enough to allow a comparison between the two methods.

Twenty-three patients had a normal radiogram and a scintigraphy evaluated as "PE +". This combination is well known from the literature (9,11). An atelectasis in a non-perfused area distal to an embolus may lead to a false negative diagnosis. Some of the patients (10/32) with old radiographic changes had ipsilateral perfusion defects, which in six cases were diagnosed as "PE -". A pulmonary embolism may be concealed even in these cases, either due to ventilatory interference from pulmonary changes or due to multiple emboli providing only small perfusion changes. This may also be the explanation for the finding of 12 patients out of 18 with radiographic "PE +" and small corresponding perfusion abnormalities in the same area, registered as "PE 0".

Most of the radiographic findings in our study (39/42) were non-specific concerning PE. A PE followed by a pulmonary infarction is likely to decrease both the perfusion and the ventilation in the affected area ("PE -") and thus escape scintigraphic detection. There were three radiograms demonstrating typical signs of infarction. Two had a normal perfusion scintigraphy and were not ventilated, the third had a Hampton´s hump (Table II) and a scintigraphic diagnosis of "PE -" due to a ventilation match.

Thus, pulmonary infarction may provide a scintigraphically false negative diagnosis of PE, which cannot be avoided unless angiography is performed.

The operative trauma and postoperative bedrest are likely to predispose for atelectases and other radiographic abnormalities found in these patients. Even if embolism often is seen together with these complications, a causal relationship was not supported by the present study.

There are several possibilities for false negative diagnoses and to a lesser extent for false positive diagnoses of PE. Although chest radiography may show signs diagnostic of PE, these signs are most often non-specific and of little value in screening of PE. A normal chest radiography does not exclude even large pulmonary emboli. The validity of a positive chest radiography is, however, considerably higher in a population with symptoms indicating PE.

To further elucidate the problems stated above, the scintigraphic coding system is presently being tested against pulmonary angiography in order to specify the borders between the diagnosis of PE and not PE.

REFERENCES

1. Nillius, S.A.; Arborelius, M., Jr; Nylander, G.: Pulmonary embolism in total hip replacement. A clinical study using ^{99m}Tc perfusion lung scan, pp. 53-69 (Thesis, University of Lund, 1978).

2. Fredin, H; Arborelius, M., Jr.: Scintigraphic evaluation of pulmonary embolism after total hip replacement, using a dry ^{99m}Tc-microaerosol for regional ventilation. Eur J Nucl Med 7:494-499 (1982).

3. Arborelius, M., Jr.: Generation of a microaerosol suitable for deposition in the peripheral airways. In: Inhalation Therapy in the Management of Airway Obstruction. Eur J Respir Dis 63:Suppl 119:19-27 (1982).

4. Fredin, H.O.; Nillius, A.S.: Fatal pulmonary embolism after total hip replacement. Acta Orthop Scand 53: 407-411 (1982).

5. Gilday, D.L.; Poulose, K.P.; DeLand, F.H.: Accuracy of detection of pulmonary embolism by lung scanning correlated with pulmonary angiography. Am J Radiol 115:732-738 (1972).

6. McNeil, B.J.: A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism. J Nucl Med 17:613-616 (1976).

7. Cheely, R.; McCartney, W.H.; Perry, J.R.; Delany, D.J.; Bustad, L.; Wynia, V.H.; Griggs, T.R.: The role of noninvasive tests versus pulmonary angiography in the diagnosis of pulmonary embolism. Am J Med 70: 17-22 (1981).

8. Goris, M.L.; Daspit, S.G.: Krypton-81m ventilation scintigraphy for the diagnosis of pulmonary emboli. Clin Nucl Med 6:207-212 (1981).

9. Biello, D.R.; Mattar, A.G.; McKnight, R.C.; Siegel B.A.: Ventilation-perfusion studies in suspected pulmonary embolism. AJR 133:1033-1037 (1979).

10. Kelley, M.J.; Elliott, L.P.: The radiologic evaluation of the patient with suspected pulmonary thromboembolic disease. Med Clin North Am 59:3-36 (1974).

11. Bell, W.R.; Simon, T.L.: Current status of pulmonary thromboembolic disease: Pathophysiology, diagnosis, prevention, and treatment. Am Heart J 103:239-262 (1982).

12. Moses, D.C.; Silver, T.M.; Bookstein, J.J.: The complementary roles of chest radiography, lung scanning, and selective pulmonary angiography in the diagnosis of pulmonary embolism. Circulation 49:179-188 (1974).

ANGIOGRAPHIC EVALUATION OF SCINTIGRAPHIC ABNORMALITIES IN THE SCREENING OF PULMONARY EMBOLISM AFTER TOTAL HIP REPLACEMENT

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SUMMARY

Of 240 consecutive patients operated upon with total hip replacement, 206 underwent perfusion scintigraphy in screening for pulmonary embolism 10 to 14 days after surgery. Seventy-seven patients with perfusion abnormalities had a supplementary ventilation scintigraphy with a dry ^{99m}Tc-microaerosol rendering images comparable to the perfusion images in all six projections. The scintigraphic abnormalities were classified according to a detailed coding system. In 50 of the 77 patients a pulmonary angiography was performed within 24 hours of the scintigraphy.

Emboli were diagnosed in all patients at locations corresponding to their largest perfusion defect with normal or slightly decreased ventilation, the types of perfusion defect being one segment (n = 6), or larger (n = 5), or multiple, sub-segmental defects larger than half a segment (n = 2). However, only two patients had emboli out of 14 with sub-segmental defects smaller than half a segment. No emboli were found in patients with only a local decrease but not complete loss of perfusion radioactivity (n = 8). No emboli were diagnosed in 27 lungs with a normal scintigraphic perfusion.

INTRODUCTION

Thromboembolic complications are common in patients undergoing total hip replacement (THR). Earlier studies at our hospital have demonstrated deep vein thrombosis of the lower limbs in approximately 60 % of the patients despite thromboembolic prevention (Nillius & Nylander 1979). These studies have also revealed scintigraphic findings indicating pulmonary embolism (PE) in about 20 % of THR patients (Nillius et al. 1978; Fredin & Arborelius 1982; Fredin et al. in press).

Scintigraphic-angiographic correlations in patients with symptoms compatible with PE indicate that whereas a normal perfusion scintigraphy practically excludes PE (Poulose et al. 1970; Greenspan 1974; Wagner & Strauss 1975; Cheely et al. 1981), there is a considerable risk of false positive diagnoses in patients with perfusion defects, especially if a ventilation scintigraphy is not added (Bogren et al. 1978; Sasahara et al. 1983). An uncritical interpretation of scintigraphic perfusion abnormalities may thus result in an unnecessary and potentially dangerous treatment with anticoagulative drugs (Robin 1977) especially in the postoperative patient.

To facilitate a more precise interpretation of perfusion scintigraphies a detailed coding system for scintigraphic abnormalities has been developed at our hospital (Fredin et al. in press).

The aim of the present investigation was to evaluate how the different scintigraphic abnormalities correlated to pulmonary angiography regarding PE.

MATERIAL

All patients who underwent total hip replacement at Malmö General Hospital during 1983 (n = 240) were considered eligible for this study. The operation was carried out mainly according to the Charnley procedure using thromboembolic prevention with dextran 70 (Macrodex^{R} 6 %

in saline or glucose, Pharmacia AB, Uppsala, Sweden). A postero-anterior and lateral chest radiography was performed preoperatively and prior to a pulmonary perfusion scintigraphy scheduled 10-14 days after surgery. Thirty-four patients either refused to participate or were early discharged from hospital. Among the 206 patients undergoing perfusion scintigraphy 129 were found to have a normal examination and were therefore excluded from the study. The remaining 77 patients (25 men and 52 women) all had perfusion abnormalities and were subjected to ventilation scintigraphy. If the angiography suite was available within 24 hours of the perfusion scintigraphy a pulmonary angiography was carried out after informed consent.

The material remaining for analysis included 50 patients (17 men and 33 women), ranging in age from 35 to 86 years (median value 71 years).

METHODS

The scintigraphic studies were carried out with a scintillation camera (Maxicamera 400, Autotom ZS, General Electric) having a parallel hole low energy collimator. The majority of the images were processed by a STAR computer (General Electric) and registered on roentgen films. Visible contrast appeared at 20 % of maximal activity and full contrast at 85 % of maximal activity. With few exceptions the patients were examined in the sitting position. Perfusion as well as ventilation images were obtained in the anterior, posterior, right and left lateral and 45° right and left posterior oblique positions.

The perfusion scintigraphy was performed after an I.V. injection of 70-100 MBq of ^{99m}Tc-MAA.

Ventilation scintigraphy was performed after inhalation of 70-100 MBq of a dry ^{99m}Tc microaerosol with a particle size of less than 0.5 μ (Arborelius 1982; Fredin & Arborelius 1982). The inhalation period was 2-5 minutes; 400 kcounts could usually be collected in less than one minute.

Fig. 1. System for coding of scintigraphic abnormalities.

Defect : No uptake of radioactivity;
Decrease : Obviously reduced but no complete loss of uptake of radioactivity.

Perfusion scintigraphy

a : A defect larger than one segment following segmental borders and pointing towards hilum or mediastinum.

b : A triangular segmental defect pointing towards hilum.

c : A triangular sub-segmental defect pointing towards hilum.

d : A defect larger than one segment with a rounded border towards hilum.

e : A peripheral defect with a rounded border towards hilum not always following segmental borders.

f : A defect at the costodiaphragmal angle with a diffuse border towards the parenchyma.

g : A segmental or larger decrease as types a or b with obvious activity out to the peripheral lung border.

h : A small, peripheral decrease.

Ventilation scintigraphy

+ : Activity normal or obviously higher than the perfusion activity in the same area.

- : Activity equal to or lower than the perfusion activity in the same area.

The ventilation study was usually made two hours after the perfusion study but postponed to the following day if the perfusion study was made in the late afternoon.

All scintigrams were primarily classified according to Fig. 1 without the knowledge of the angiographic results.

Bilateral selective pulmonary angiography was performed after percutaneous catheterization of the femoral vein with a 5 F pigtail catheter (Cook Inc., Bloomingdale, Ind., USA) with six side-holes. The contrast media used were iohexol (Omnipaque, Nyegaard & Co., Oslo), sodium/meglumine/calcium metrizoate (Isopaque Coronar, Nyegaard & Co.) or meglumine/sodium ioxaglate (Hexabrix, Laboratoire Guerbet, Paris). All contrast media were pre-heated to a temperature of +37°C and 45 ml injected at a concentration of 300 mg I/ml and a rate of 25 ml/s in each pulmonary artery. In 10 patients conventional serial cut-films were obtained at a rate of three films per second for four seconds and one film per second for another four seconds. In the remaining 40 patients cine-recording was performed using a Siemens Angioscope with a 30 cm image intensifier and a frame-rate of 50/s. A simultaneous video-recording was made to monitor the diagnostic quality. Recordings were obtained in the postero-anterior and lateral or oblique projections. If oblique views were used, the right and left lungs were examined in the 45-55° left and right anterior oblique projections, respectively. When indicated, supplementary examinations were made with magnification and superselective injections of 25-30 ml of contrast medium in the right interlobar or left lower lobe artery. The pulmonary arterial pressure was recorded before and after each injection. All patients were ECG monitored during the examination.

Using the results of the scintigraphy the angiograms were evaluated by two radiologists with regard to signs of embolism, i.e. clear-cut obstructions of pulmonary arterial branches or intravascular filling defects. The emboli were classified as occlusive or almost occlusive if no or markedly delayed contrast filling was registered peripheral to the embolus, and as non-occlusive if no obvious delay of the peripheral contrast filling was demonstrated.

The nurses' daily records were retrospectively scrutinized for notes of postoperative attacks of sudden chest pain.

A comparison of scintigraphic and angiographic findings of PE was made for each patient. A more detailed correlation was also made for each lung and each lobe. The lingula was considered as a separate lobe in order to make the correlation in the left lung more precise.

RESULTS

Nineteen patients had PE at angiography. Eight of these had emboli involving five or more segmental arteries, eight involving two to four, whereas two patients had emboli involving a single segmental artery and one an embolus involving a sub-segmental artery. Postoperative chest pain differed significantly ($p < 0.05$) between patients with emboli and those without. Six patients with emboli had chest pain, four of the six had emboli involving more than four segmental arteries. Seven of the 13 patients without chest pain had emboli involving four segmental arteries or more. No patient without PE had chest pain postoperatively. The correlation between scintigraphic and angiographic findings is presented in Table I.

Perfusion abnormalities with ventilation code (+) (Fig. 1)

Fifteen of the 32 patients in this group had PE at angiography. Eleven patients with their largest perfusion defect of types a, b or d all had PE at corresponding locations. Among six patients with a perfusion defect type c two had PE at corresponding locations, both had two subsegmental defects larger than half a segment which corresponded to the site of the emboli. The remaining four patients all had sub-segmental defects smaller than half a segment. In three of them this was the only recognizable defect. Of nine patients with their largest perfusion defect type e, two had PE - one at the same location as the embolus. No PE was found among six patients with their largest perfusion abnormalities of codes f, g and h.

TABLE I

Correlation between perfusion/ventilation scintigraphy and bilateral, selective pulmonary angiography in 50 patients with scintigraphic perfusion abnormalities. The scintigraphic codes correspond to the type of abnormality presented in Fig. 1, the figures to the number of patients.

Perfusion	Ventilation			
(type of largest abnormality)	+		-	
	PE	No PE	PE	No PE
a	4*		1*	1
b	6*		1*	2
c	2*>	4<	1°	2
d	1*			1
e	1*,1°	7	1°	3
f		1		2
g		4		2
h		1		1
Total	15	17	4	14

PE = Pulmonary embolus at angiography;

No PE = No pulmonary embolus at angiography;

* = PE and largest perfusion abnormality at corresponding locations;

° = PE and largest perfusion abnormality at different locations;

> = perfusion defect larger than half a segment;

< = perfusion defect smaller than half a segment.

Perfusion abnormalities with ventilation code (-) (Fig. 1)

Four of the 18 patients in this group had PE at angiography.

Three patients out of the nine with their largest perfusion defects of types a, b, c or d, had PE. The patients with defects of types a or b had emboli at corresponding locations whereas one patient with two defects of type c had PE at another location. In this patient angiography, performed the day after the scintigraphy, demonstrated normal blood flow beyond the embolus.

One patient out of the four with their largest perfusion defects of type e was demonstrated to have PE. He had multiple e defects in his upper lobes. Angiography revealed non-occluding emboli in his left lower lobe.

No PE was found in the remaining five patients with their largest perfusion abnormality of types f, g and h.

All patients with PE in this group had normal chest radiography.

Relevance of normal perfusion scintigraphy for separate lungs and lobes

Normal perfusion in one of the lungs was found at scintigraphy in 27 patients. Angiography did not demonstrate emboli in any of these lungs.

Out of 300 lobes in 50 patients, 201 were normally perfused. Emboli were diagnosed at angiography in 18 of these lobes (11 patients). In 11 lobes the embolus engaged more than one segment. In five of the 18 lobes (5 patients) angiography was performed on the same day as the scintigraphy without evidence of impeded blood flow. In the remaining 13 lobes (6 patients) angiography was performed on the following day with normal blood flow in seven lobes and a notably reduced or occluded lumen of the vessel in the other six lobes.

Eight of 11 patients with emboli in areas with scintigraphically normal perfusion also had emboli in other areas corresponding to perfusion defects larger than half a segment with a ventilation code (+).

Pulmonary arterial pressure and complications

The mean pulmonary arterial pressure before injection of contrast medium ranged from 5 to 32 mm Hg (median value 14). After the angiography the mean pressure ranged from 13 to 39 mm Hg (median value 20). The rise in mean pulmonary arterial pressure during examination ranged from 0 to 19 mm Hg (median value 8).

One patient developed transient chest pain towards the end of the angiography. No complications were registered.

DISCUSSION

Most data on the value and limitations of perfusion/ventilation scintigraphy in the diagnosis of acute pulmonary embolism are based on retrospective analyses of non-consecutive series of symptomatic patients using ^{133}Xe for the ventilation scintigraphy (Moses et al. 1974; McNeil 1976; Bogren et al. 1978; Biello et al. 1979 a; Cheely et al. 1981; Sostman et al. 1983).

The patients of the present investigation were prospectively selected from a consecutive series of postoperative patients known to have a high incidence of thromboembolic complications with few symptoms and signs. A detailed coding system for definition of perfusion/ ventilation abnormalities was applied with the aim of producing a consistent scintigraphic evaluation. Ventilation scintigraphy was performed with a dry ^{99m}Tc-microaerosol permitting multiple images in the same pro-

jections and with the same spatial resolution as the perfusion scintigrams (Arborelius 1982; Fredin & Arborelius 1982). Furthermore, the subsequent pulmonary angiographies were performed within 24 hours.

Pulmonary angiography is accepted as the most specific method for diagnosing pulmonary embolism (Bookstein 1969; Bookstein & Silver 1974; Dalen et al. 1971; Moses et al. 1974; Novelline et al. 1978) even though its absolute accuracy has been difficult to evaluate. The technique is fairly expensive and has a morbidity rate of about 5 % and a mortality rate of about 0.5 % (Dalen et al. 1971; Moses et al. 1974; Mills et al. 1980). Therefore, it cannot be used in a screening procedure.

Two angiographic criteria are considered diagnostic of pulmonary embolism: a constant intraluminal filling defect on multiple films and sharp cut-offs of vessels (Bookstein 1969; Bookstein & Silver 1974; Dalen et al. 1971). Other signs such as oligemia, poor filling of small vessels, pruning of vessels and asymmetric flow are non-specific and may occur in a variety of lung disorders and in pulmonary hypertension (Dalen et al. 1971; Bookstein & Silver 1974). This means that small peripheral emboli may escape detection but still cause scintigraphic perfusion defects. Also, larger emboli may escape detection if the quality of the angiographic examination is poor due to insufficient patient cooperation or if the technique does not include bilateral selective injections with sufficient amounts of contrast medium at a sufficient rate and, when required, a supplement with superselective injections and magnification. The less toxic effects of the low osmolality contrast media iohexol and ioxaglate also permit larger contrast doses to be injected with less risk to the patient as compared with the high osmolality metrizoate. Furthermore, the low osmolality contrast media in our experience provoke coughing much less frequently, thereby reducing the risk of blurring, which is important, especially when the serial cut-film technique is used.

Perfusion abnormalities with normal or almost normal ventilation are usually considered to be diagnostic of PE (McNeil 1976; Biello et al. 1979 a; Cheely et al. 1981; Goris & Daspit 1981; Hull et al. 1983) provided the defects involve at least one full segment. Sostman et al. (1983), however, suggest that also sub-segmental defects may be accepted, but only if there are two or more segmental defects present or "segmental equivalents" (one segment = two sub-segments). In the present study there was agreement between scintigraphy and angiography in 10 out of 10 patients with large triangular, segmental or larger, perfusion defects. In these cases there was also a correspondence in site between the findings of the two methods.

Biello et al. (1979 a) also found a high probability of PE when multiple moderate-sized sub-segmental defects (25 to 75 % of a segment volume) were present whereas other authors, without defining the size of the sub-segmental defects, found a probability varying from 4 out of 15 (Hull et al. 1983) to 4 out of 5 patients (Goris & Daspit 1981). Two of our patients each had two large triangular sub-segmental defects, i.e. one "segmental equivalent", with emboli at the same sites, whereas only 2 had emboli out of 14 with small sub-segmental defects (small c, e and f).

The variation in opinions regarding the probability of PE related to size of the perfusion defects may be explained by different angiographic techniques and the use of different isotopes for the ventilation studies. Due to their superior spatial resolution, ^{81}Kr (Goris & Daspit 1981) and ^{99m}Tc-microaerosol may reveal smaller ventilation abnormalities than ^{133}Xe (Hull et al. 1983). Hence, the number of "normally ventilated" perfusion defects combined with normal angiography may be reduced.

Perfusion/ventilation scintigraphies with perfusion abnormalities corresponding in size and location to areas with a significantly decreased ventilation as the only finding were regarded as inconclusive, since a variety of lung disorders causing decreased ventilation also result in

perfusion abnormalities indistinguishable from those caused by emboli (Biello et al. 1979 a,b; Alderson et al. 1981; Sostman et al. 1983). Acute pulmonary embolism may also cause decreased ventilation secondary to bronchoconstriction (Gurewich et al. 1963; Thomas et al. 1964; Isawa et al. 1972), although rarely detected by ^{133}Xe studies (Kessler & McNeil 1975; Epstein et al. 1976; Alderson et al. 1978). Whether ^{99m}Tc is more sensitive in this respect is not known.

Abnormal perfusion/ventilation scintigraphies have been reported to be associated with emboli in 0 to 30 % of the patients (McNeil 1976; Biello et al. 1979 a; Sostman et al. 1983). These variations are probably related to bias in the patient selection. In the present investigation including patients with a relatively high risk of asymptomatic pulmonary embolism, emboli were demonstrated in four of the 15 patients with any type of abnormally ventilated perfusion defect. One of these four patients had diffuse obstructive lung disease with multiple perfusion/ventilation abnormalities in both lungs and multiple emboli bilaterally. Another patient had a single, segmental perfusion defect, abnormally ventilated, with an occluding embolus in the corresponding segmental artery. This might thus represent bronchospasm induced by an embolus. The remaining two patients each had two small peripheral defects and a single non-occlusive embolus in a normally perfused area.

Perfusion scintigraphies with single abnormalities independent of type and ventilation were combined with emboli in only three of 23 patients, whereas 16 had emboli among the 27 patients with multiple abnormalities. This difference is significant and in accordance with the findings by Sostman et al. (1983).

Almost 10 % of normally perfused lobes in our material had emboli at angiography. Many of these emboli were found to be non-occlusive. All patients with occlusive emboli had angiography the day after the scintigraphy which implies that embolization may have occurred later. Despite this lack of correspondence between scintigraphy and angio-

graphy at a particular site, the high sensitivity of perfusion scintigraphy is probably due to the fact that the great majority of patients have multiple emboli (Sostman et al. 1983).

Our finding that 27 patients with one normally perfused lung all had a normal angiography of that lung is in accordance with the concept that a normal perfusion scintigraphy practically excludes pulmonary embolism (Bell & Simon 1982). Furthermore, it implies that when evaluating unilateral scintigraphic abnormalities with angiography, selective injections in the normally perfused lung may be avoided, especially in patients to whom the examination carries a potential risk.

Although chest pain and shortness of breath are highly indicative of pulmonary embolism in the postoperative patient the majority of patients with emboli were asymptomatic. It should also be noted that half of the asymptomatic patients had pulmonary embolism of the same magnitude as the patients with symptoms, i.e. emboli in three segmental arteries or more.

CONCLUSIONS

Based on earlier reports and on the present investigation, the following conclusions can be made regarding scintigraphic evaluation in the screening of postoperative patients for pulmonary embolism.

(1) Triangular perfusion defects with a size of at least one segment without significantly decreased ventilation have a high probability of PE.

(2) Single or multiple large sub-segmental (> 50 %) triangular perfusion defects without significantly decreased ventilation require further scintigraphic/angiographic studies to document their probablity of PE.

(3) Small sub-segmental (< 50 %) perfusion defects and areas with a decreased perfusion but without complete loss of perfusion have a low probability of PE.

(4) Perfusion defects combined with significantly reduced ventilation are an inconclusive finding regarding PE. Further analyses are needed to determine the diagnosis.

REFERENCES

ALDERSON P.O., BIELLO D.R., SACHARIAH K.G. and SIEGEL B.A.: Scintigraphic detection of pulmonary embolism in patients with obstructive pulmonary disease. Radiology 138 (1981), 661.

ALDERSON P.O., DOPPMAN J.L., DIAMOND S.S., MENDENHALL K.G., BARRON E.L. and GIRTON M.: Ventilation-perfusion lung imaging and selective pulmonary angiography in dogs with experimental pulmonary embolism. J Nucl Med 19 (1978), 164.

ARBORELIUS M., JR.: Generation of a microaerosol suitable for deposition in the peripheral airways. Eur J Respir Dis 63:(Suppl) 119 (1982), 19.

BELL W.R. and SIMON T.L.: Current status of pulmonary thromboembolic disease: Pathophysiology, diagnosis, prevention, and treatment. Am Heart J 103 (1982), 239.

BIELLO D.R., MATTAR A.G., McKNIGHT R.C. and SIEGEL B.A.: Ventilation-perfusion studies in suspected pulmonary embolism. AJR 133 (1979 a), 1033.

BIELLO D.R., MATTAR A.G., OSEI-WUSU A., ALDERSON P.O., McNEIL B.J. and SIEGEL B.A.: Interpretation of indeterminate lung scintigrams. Radiology 133 (1979 b), 189.

BOGREN H.G., BERMAN D.S., VISMARA L.A. and MASON D.T.: Lung ventilation-perfusion scintigraphy in pulmonary embolism. Diagnostic specificity compared to pulmonary angiography. Acta Radiol Diagn (Stockh) 19 (1978), 933.

BOOKSTEIN J.J.: Segmental arteriography in pulmonary embolism. Radiology 93 (1969), 1007.

BOOKSTEIN J.J. and SILVER T.M.: The angiographic differential diagnosis of acute pulmonary embolism. Radiology 110 (1974), 25.

CHEELY R., McCARTNEY W.H., PERRY J.R., DELANY D.J., BUSTAD L., WYNIA V.H. and GRIGGS T.R.: The role of noninvasive tests versus pulmonary angiography in the diagnosis of pulmonary embolism. Am J Med 70 (1981), 17.

DALEN J.E., BROOKS H.L., JOHNSON L.W., MEISTER S.G., SZUCS M.M., JR., DEXTER L.: Pulmonary angiography in acute pulmonary embolism: Indications, techniques, and results in 367 patients. Am Heart J 81 (1971), 175.

EPSTEIN J., TAYLOR A., ALAZRAKI N. and COEL M.: Acute pulmonary embolus associated with transient ventilatory defect: Case report. J Nucl Med 16 (1976), 1017.

FREDIN H. and ARBORELIUS M., JR.: Scintigraphic evaluation of pulmonary embolism after total hip replacement, using a dry ^{99m}Tc-microaerosol for regional ventilation. Eur J Nucl Med 7 (1982), 494.

FREDIN H., ARBORELIUS M., JR. and HELLEKANT C.: Scintigraphy and chest radiography in the screening of pulmonary embolism after total hip replacement. Respiration (in press).

GORIS M.L. and DASPIT S.G.: Krypton-81m ventilation scintigraphy for the diagnosis of pulmonary emboli. Clin Nucl Med 6 (1981), 207.

GREENSPAN R.H.: Does a normal isotope perfusion scan exclude pulmonary embolism? Invest Radiol 9 (1974), 44.

GUREWICH V., THOMAS D., STEIN M. and WESSLER S.: Bronchoconstriction in the presence of pulmonary embolism. Circulation 27 (1963), 339.

HULL R.D. et al.: Pulmonary angiography, ventilation lung scanning, and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. Ann Intern Med 98 (1983), 891.

ISAWA T., TAPLIN G.V., BEAZELL J. and CRILEY J.M.: Experimental unilateral pulmonary artery occlusion. Acute and chronic effects on relative inhalation and perfusion. Radiology 102 (1972), 101.

KESSLER R.M. and McNEIL B.J.: Impaired ventilation in a patient with angiographically demonstrated pulmonary emboli. Radiology 114 (1975), 111.

McNEIL B.J.: A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism. J Nucl Med 17 (1976), 613.

MILLS S.R., JACKSON D.C., OLDER R.A., HEASTON D.K. and MOORE A.V.: The incidence, etiologies, and avoidance of complications of pulmonary angiography in a large series. Radiology 136 (1980), 295.

MOSES D.C., SILVER, T.M. and BOOKSTEIN J.J.: The complementary roles of chest radiography, lung scanning, and selective pulmonary angiography in the diagnosis of pulmonary embolism. Circulation 49 (1974), 179.

NILLIUS S.A., ARBORELIUS M., JR. and NYLANDER G.: Pulmonary embolism in total hip replacement. A clinical study using $^{99}Tc^{m}$ perfusion lung scan, p. 53, Thesis, University of Lund, 1978.

NILLIUS S.A. and NYLANDER G.: Deep vein thrombosis after total hip replacement: A clinical and phlebographic study. Br J Surg 66 (1979), 324.

NOVELLINE R.A., BALTAROWICH O.H., ATHANASOULIS C.A., WALTMAN A.C., GREENFIELD A.J. and McKUSICK K.A.: The clinical course of patients with suspected pulmonary embolism and a negative pulmonary arteriogram. Radiology 126 (1978), 561.

POULOSE K.P., REBA R.C., GILDAY D.L., DELAND F.H. and WAGNER H.N., JR.: Diagnosis of pulmonary embolism. A correlative study of the clinical, scan, and angiographic findings. Br Med J 3 (1970), 67.

ROBIN E.D.: Overdiagnosis and overtreatment of pulmonary embolism: The emperor may have no clothes. Ann Intern Med 87 (1977), 775.

SASAHARA A.A., SHARMA G.V.R.K., BARSAMIAN E.M., SCHOOLMAN M. and CELLA G.: Pulmonary thromboembolism. Diagnosis and treatment. JAMA 249 (1983), 2945.

SOSTMAN H.D., RAPOPORT S., GLICKMAN M.G. and GOTTSCHALK A.: Problems in noninvasive imaging of pulmonary embolism. Radiol Clin North Am 21 (1983), 759.

THOMAS D., STEIN M., TANABE G., REGE V. and WESSLER S.: Mechanism of bronchoconstriction produced by thromboemboli in dogs. Am J Physiol 206 (1964), 1207.

WAGNER H.N., JR. and STRAUSS H.W.: Radioactive tracers in the differential diagnosis of pulmonary embolism. Prog Cardiovasc Dis 17 (1975), 271.

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